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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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SURGERY

VOL. 26 OCTOBER, 1949 No. 4

Original Communications

THE TREATMENT OF ADVANCED MAMMARY CANCER WITH ESTROGENS

MAX CUTLER, M.D., MELVIN SCHLEMENSON, M.D.,* AND JOHN J. KEARNEY, M.D., CHICAGO, ILL., AND EDUARDO CACERES, M.D., LIMA, PERU

(From the Chicago Tumor Institute)

THE purpose of this paper is to record the results in 20 consecutive cases of advanced cancer of the breast treated with estrogens.

Since its isolation in 1923, the growth-stimulating properties of the follicular hormone have been well established and generally accepted.[1, 2, 3] In 1942, a group of English investigators demonstrated the growth-inhibiting effects of estrogens in laboratory animals.[4] This led to the use of estrogens in human beings with advanced mammary cancer. Haddow and his group,[5] in 1944, reported palliative results in 10 of 22 cases of advanced breast cancer treated with triphenyl-chloroethylene and in 5 of 14 cases treated with stilbestrol. The favorable effects were confined almost exclusively to the older age group. In addition, Koller[6] (a member of Haddow's group) described microscopic changes which occurred during estrogen therapy. In the same year, several groups of English investigators presented 168 cases of advanced breast cancer treated with stilbestrol[7] with the results shown in Table I.

Nathanson[8] has treated over 150 cases with various estrogens at the Massachusetts General Hospital. The results in isolated cases have been published,[9, 10, 11] but no detailed report has as yet appeared. Herrman, Adair, and Woodard[12] treated 17 cases with ethinyl estradiol and noted favorable responses in 7.

CASE REPORTS

Twenty patients were treated. Thirteen were not benefited and the disease progressed; metastases to bone were present in 4 of these 13 and in 1 of the other 7; 1 patient demonstrated improvement in a bone lesion. In 7 cases there was definite improvement; in 3, the disease was temporarily arrested and a marked improvement in the general condition was observed; in 4, ulcers of the breast healed, and in 1 of these, metastasis to a lumbar vertebra showed deposition of calcium.

Large doses of both synthetic and natural estrogenic substances were used: diethylstilbestrol monomethyl ether (Monomestrol†), stilbestrol (oral and intramuscular), and a solution of estrogens in oil, principally estrone (intramuscu-

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†Wallace & Tiernan Products, Inc., Belleville, N. J.

TABLE I

AGE (YR.)	NUMBER	IMPROVED	NO IMPROVEMENT	SPECTACULAR IMPROVEMENT
Under 60	100	14	86	1
Over 60	68	27	41	5
Total	168	41	127	6

lar). The relative potency of the principal estrogenic substances has been recorded elsewhere.[13] No essential difference in response was noted in the doses given, and vaginal smears demonstrated the follicular phase of the menstrual cycle in all patients treated.

The details of the four cases which showed objective evidence of palliation are recorded here.

CASE 1.—I. M., a woman, aged 74 years, had a radical mastectomy for cancer in 1936. Local skin recurrences were removed surgically on four different occasions and another, in September, 1947, was treated with x-rays. On admission, March 25, 1948, there was an ulcer 9 by 4 cm. in the mastectomy scar; in addition, there were palpable nodes in the supraclavicular and infraclavicular areas. No metastasis was seen in the lungs or pelvis. Biopsy examination of the ulcer showed carcinoma. Beginning March 25, 1948, she received 7 mg. of a solution of estrogens in oil* intramuscularly twice weekly. The ulcerated lesion on the chest wall became smaller and there was active epithelial proliferation. The supraclavicular mass regressed and the patient felt well and gained weight. There was one episode of vaginal bleeding which lasted for two days during therapy. On Aug. 9, 1948, there was further regression of the lesion on the chest wall and the patient felt well. She received 252 mg. of estrogenic substance, and treatment is continuing.

Comment.—The slow but progressive healing of a carcinomatous ulcer is demonstrated, and the necessity for continuing treatment over a number of months is indicated.

CASE 2.—E. H., a woman, aged 76 years, was admitted on March 9, 1948, complaining of a mass in the left breast for four years and ulceration for over two years. There was a mass 9 by 7 cm. in the upper, outer portion of the left breast with a 5.5 by 5 cm. area of ulceration and the breast was distorted (Fig. 1). Hard nodes were palpable in the axilla. There was no metastasis in the lungs. Biopsy examination of the ulcer disclosed carcinoma. Between March 9, 1948, and April 26, 1948, she received 10 mg. of a solution of estrogens in oil intramuscularly twice weekly. Because of vaginal bleeding, the dose was reduced in 5 mg. twice weekly on April 26, and continued at that rate. There was complete healing of the ulcer on April 4, 1948. On June 10, 1948, the mass had regressed further and the ulcerated area was replaced by a thick scar (Fig. 2). Serial biopsy examinations showed significant microscopic changes. The general condition of the patient is good and the mass continues to regress. Further regression of the mass was evident at the last examination on July 23, 1948. The patient has received a total of 260 mg. of estrogenic substance, and treatment is continuing.

Comment.—The thick scar is a gross example of the extensive fibrous tissue proliferation which is seen microscopically in some cases.

CASE 3.—A. M., a woman, aged 76 years, was treated with telecurietherapy for a cancer of the right breast in 1942. The mass regressed and then began to grow slowly. The patient refused any further treatment. When seen on April 5, 1948, the mass had ulcerated. Biopsy examination showed carcinoma. There was no metastasis. Beginning April 5, 1948, she received 5 mg. of estradiol dipropionate intramuscularly twice weekly, and the ulcer began to

*Lakeside Laboratories, Inc., Milwaukee, Wis.

heal rapidly. She then developed signs of cardiac decompensation and was treated with digitalis. On June 6, 1948, there was complete healing of the ulcer and regression of the underlying mass; the patient then became irregular in reporting for treatment and on July 9, 1948, the lesion had again ulcerated and the disease was progressing. After the patient was persuaded to resume regular treatment, the ulcer again healed and on Aug. 3, 1948, the disease appeared stationary. The patient has received 140 mg. of estradiol dipropionate and treatment is continuing.

Fig. 1.

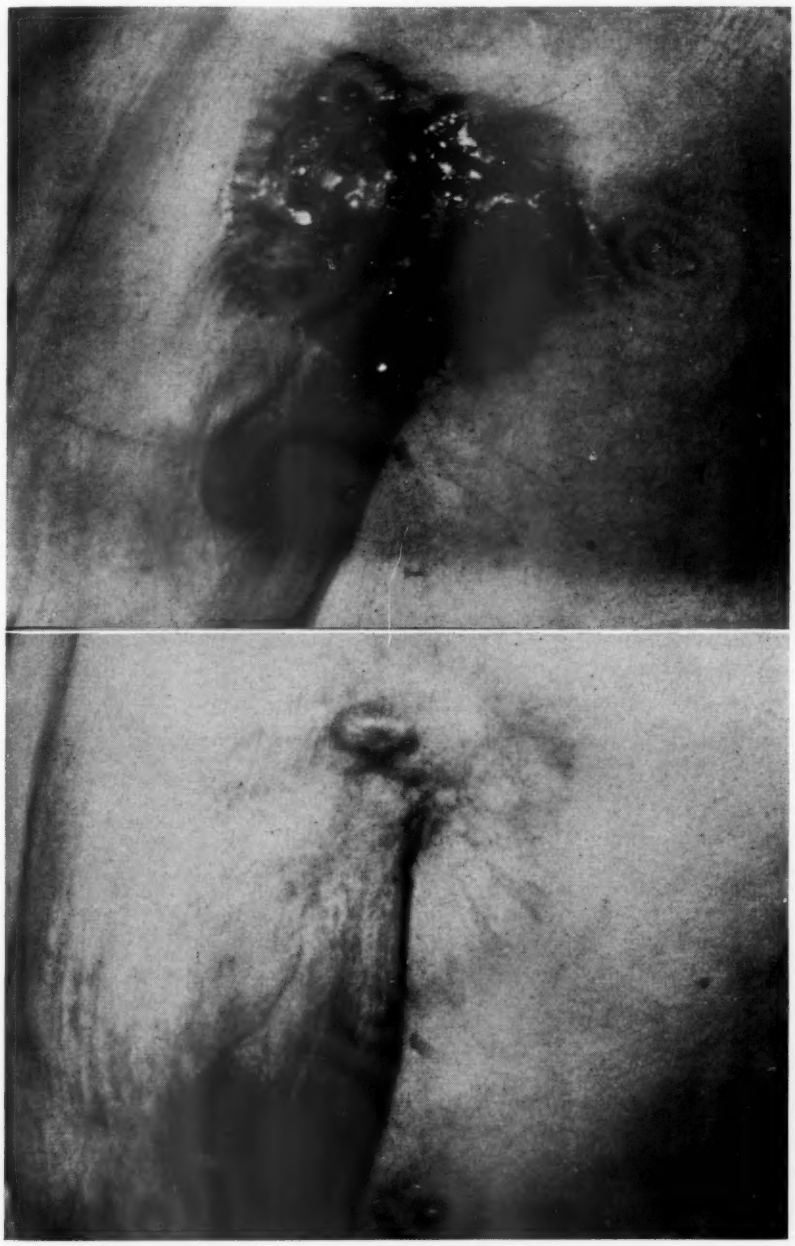
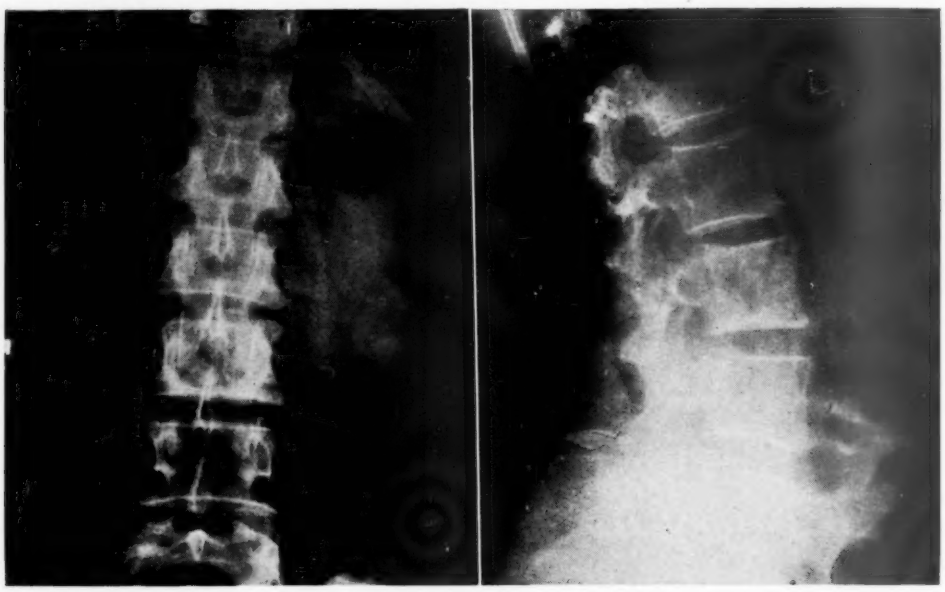


Fig. 2.

Fig. 1 (Case 2).—Before treatment.
Fig. 2 (Case 2).—After treatment.

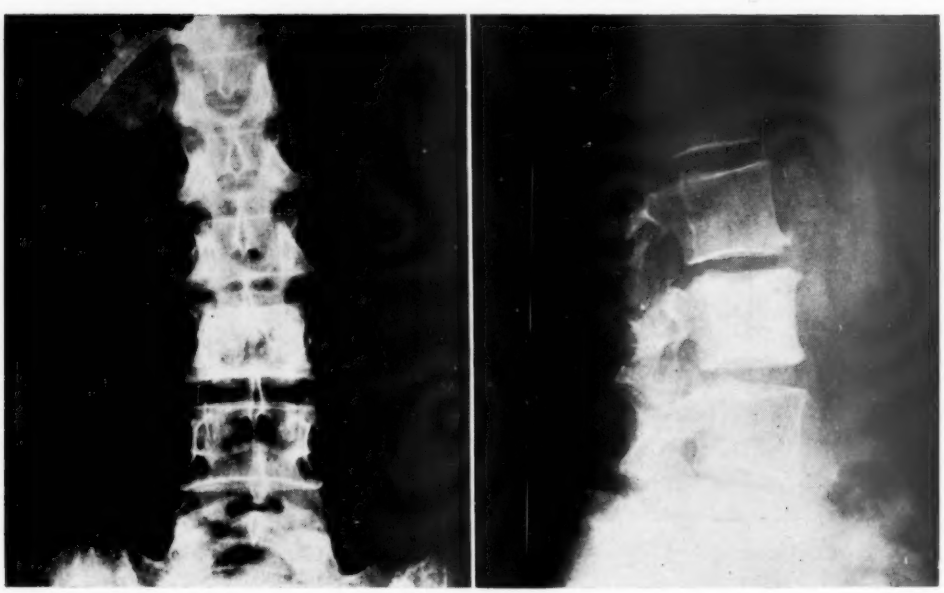
Comment.—The duplication of the initial response to estrogen therapy demonstrates that the healing of an ulcer is not the end point in a reaction and that regular treatment is indicated thereafter until recrudescence of the disease takes place and should be continued until it is established whether further aid is or is not to be obtained.

CASE 4.—S. E., a woman, aged 75 years, was admitted on May 14, 1948. In 1943, a cancer of the left breast had been treated with removable radium needles with complete regression of the mass; in February, 1948, an ulcerated mass appeared in the treated



A. *B.*

Fig. 3 (Case 4).—Before treatment.



A. *B.*

Fig. 4 (Case 4).—After treatment.

area. On admission, May 14, 1948, there was an area of ulceration 8 by 8 cm. in the upper, outer quadrant of the left breast and a hard mass in the left axilla. In addition, there was a mass in the right breast characteristic of cancer and hard nodes in the right axilla and left supraclavicular area. There was no metastasis in the lungs. An osteolytic area was seen in the fourth lumbar vertebra (Fig. 3, *A* and *B*). Biopsy examination of the ulcerated area disclosed carcinoma. The patient received 15 mg. of stilbestrol orally daily. The ulcerated area showed progressive healing and the general condition of the patient improved. On Aug. 9, 1948, there was regression of the metastatic nodes and almost complete healing of the ulcerated area. Deposition of calcium in the bone metastasis was manifest (Fig. 4, *A* and *B*). The patient has received 1,120 mg. of stilbestrol, and treatment is continuing.

Comment.--This case illustrates the healing of a carcinomatous ulcer and the concomitant improvement in a bone metastasis.

DISCUSSION

The physiologic effects of estrogen are well known. Patients under treatment with large doses occasionally develop other manifestations including deep pigmentation of the areola, uterine bleeding (during or following treatment), softening of the skin, and generalized edema. This latter effect probably results from disturbance of the electrolyte balance.[14] Toxic effects such as nausea, vomiting, and abdominal cramps occur occasionally, but usually are controlled by interrupting the medication or by changing to another estrogen; however, we have seen several patients who were unable to tolerate large doses of estrogens in any form.

The general scheme of response follows a pattern similar to that reported in the English study.[7] It appears that palliation can be expected most frequently in patients over 60 years of age and in a relatively small number of patients under 60 years. The relationship of response to age is tabulated in Table II.

TABLE II

AGE (YR.)	IMPROVED	NOT IMPROVED	TOTAL
Over 60	5	3	8
Under 60	2	10	12
Total	7	13	20

The exact duration of palliation in our cases cannot be discussed at this time as the patients have not been observed long enough. It is our impression that the improvement is only temporary.

We are continuing the medication in all of the cases which respond favorably until the palliative effect is no longer evident. In this way, the duration of response will be determined. More precise information will be forthcoming from a study being conducted by the Therapeutic Trials Committee of the American Medical Association.

Although we have no evidence that the disease was accelerated in any case, it has been suggested that this may occur in young women[12] and estrogen must be used cautiously in that group.

SUMMARY AND CONCLUSIONS

1. Twenty consecutive cases of advanced cancer of the breast were treated with estrogenic substances; palliative effects were observed in seven.

2. The palliation occurred most frequently in the patients over 60 years of age.

3. The effect was evident in both bone and soft-tissue metastases.

4. Several estrogenic substances were used, but no difference in response was noted. The optimal doses have not been established.

5. Vaginal bleeding occurred in some patients.

6. The duration of palliation has not as yet been determined.

7. It is our impression that certain patients with advanced cancer of the breast experience relief from pain and a sense of well-being during estrogen therapy, even in the absence of objective improvement.

8. No evidence that estrogens can cure cancer of the breast was found.

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A MAMMAPLASTIC SUBSTITUTE FOR AMPUTATION IN HYPERTROPHIES

JACQUES W. MALINIAC, M.D., NEW YORK, N. Y.

GENERAL CONSIDERATIONS

THE following modification of the classical retromammary procedures has proved a satisfactory substitute for mammectomy with free grafting of the nipple in several types of massive hypertrophy. It is particularly indicated when reduction of the anteroposterior diameter of the breast is the chief objective and retention of sensitivity in the nipple is an important consideration.[1] It cannot be employed when the areola is greatly enlarged.

The retromammary approach was first described by Thomas[2] and Warren[3] for the removal of benign tumors. Subsequently Guinard[4] and Morestin[5] followed this route for plastic excision in breast hypertrophies. Apparently none of these authors recognized the necessity for plastic reconstruction of the skin covering to impart proper form, and adequate mastopexy to ensure permanence of results.

The great advantage of the submammary route lies in its safety. It permits wide exposure of the posterior aspect of the breast and extensive glandular resection without jeopardy to the main mammary blood supply and its periareolar ramifications[6] (Fig. 1). It also facilitates affixation of the breast to the pectoral muscle.

Because of its safety factors, this procedure can often be carried out in one stage. However, two stages are preferable, allowing greater attention to fine detail in the pursuit of an optimum end result.

PROCEDURE

Glandular Resections.—An incision is made in the submammary fold, through which the posterior surface of the breast is bluntly separated along the retromammary aponeurosis as far as the second intercostal space. The breast is then turned over on the chest and its posterior aspect exposed for glandular resection. The type of excision varies with the nature and degree of the hypertrophy (Fig. 2).

Reduction of the gland is effected in such manner as to preserve the bulk of its central portion. Excisions are made in the external and lower quadrants, where enlargement is usually greatest. As a rule bleeding is minimal because of the disposition of the blood supply; the surgical area can be shaped without danger of interference with the main vascularization of the nipple.

In enlargements associated with isolated benign tumors (cysts, fibroadenomas, etc.), a number of V-shaped segments can be taken from the entire thickness of the gland, each including one or more growths. No attempt is made to decapsulate cysts as they are usually adherent to the surrounding tissue and may open during the process of separation. If the breast appears

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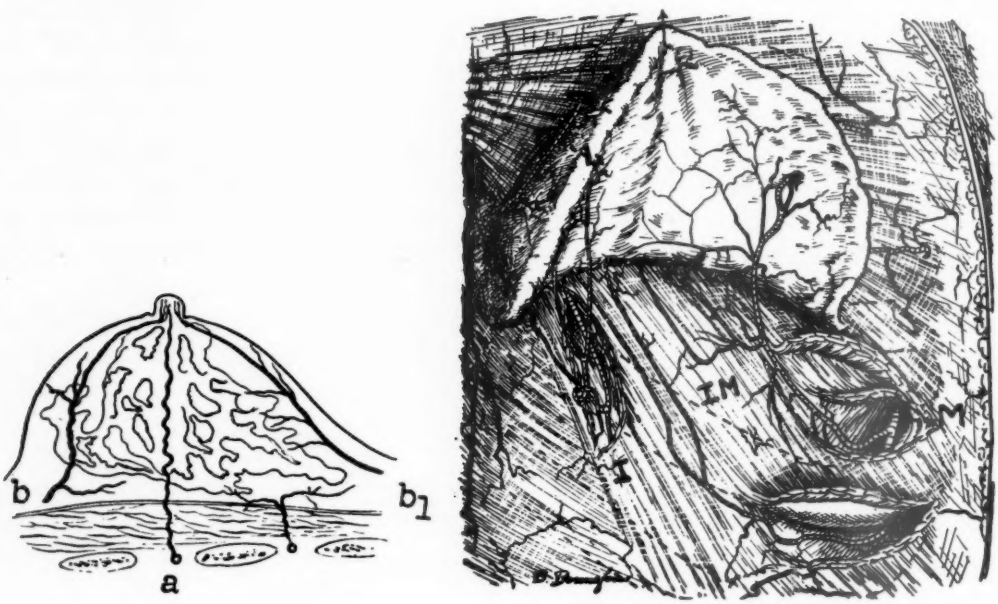
undesirably flat, the radial sections of the gland should be overlapped before suturing to produce conical protrusion.

Mastopexy.—Firm affixation of the reconstructed breast is an essential element in this as in all mammaplastic procedures. The distended, atrophied skin cannot be relied upon to maintain the organ in position even when a proper skin plastic is done. Absorbable sutures are also unreliable. To counteract the natural tendency of the breast to descend, resilient nonabsorbable suture material should be used.

The discarded excess skin affords an ideal substance for this purpose. A strip of suitable size is placed under traction and the epithelium shaved off with a skin-graft knife. Three or four strips, eight to ten inches long and one-third inch wide, usually suffice for firm affixation (Fig. 3). No other nonabsorbable material offers as great assurance of permanence and as little risk in the poorly vascularized, friable tissue of this area.



A. *B.*

Fig. 1.—Blood supply, posterior aspect of breast. *A*, Sagittal horizontal section, showing main perforating vessels and their branches (*b*, b_1) in subcutaneous structures, at levels varying from 0.5 to 2.5 cm. according to amount of fat. These must be retained. (*a*) The relatively unimportant intercostals, penetrating gland from behind and playing unessential role in supply of nipple. (The direct penetration of nipple shown here is rare.)
B, Main retromammary arteries (*IM*) originate in internal mammary artery (*M*). The less important intercostals (*I*) derive from aorta. These long vessels are easily separated in retromammary resection. (Salmon.)

The dermal loops are inserted vertically through gland and pectoral muscle with a long fascia needle; catgut sutures secure the knots in place. The loops are placed to the side of the midline so as to cause the middle segment of the breast to protrude in cone shape.

Skin Plastic.—Following reduction and affixation of the gland, the skin covering must be adjusted to conform to the reduced breast (Fig. 4). One of the chief disadvantages of a retromammary procedure is the flatness resulting from failure to do this. Wide lateral undermining of the flaps, accompanied

by adequate excision in both vertical and horizontal diameters, is required for even distribution of the skin. Ample fatty padding of the lateral flaps should be retained beyond the areolar zone.

When protuberance of the breast is the chief problem, retromammary resection may suffice for repair without a skin plastic.

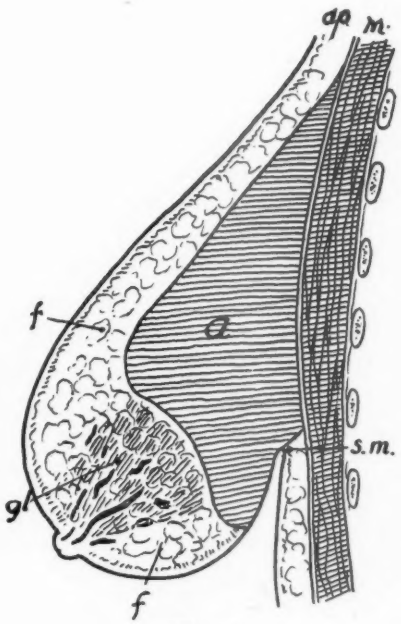


Fig. 2.

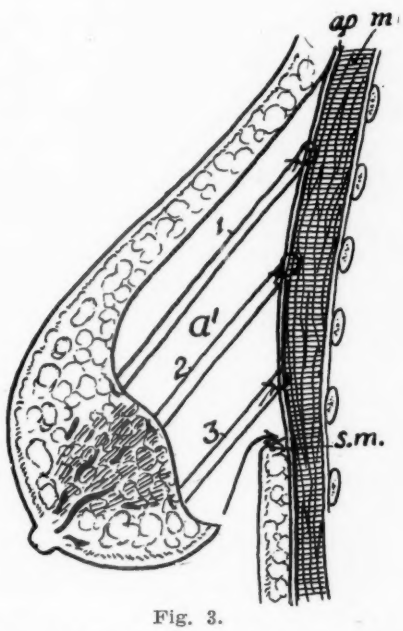
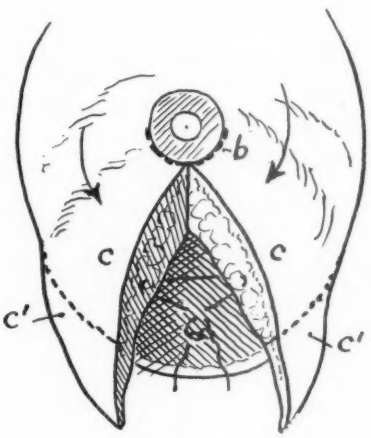


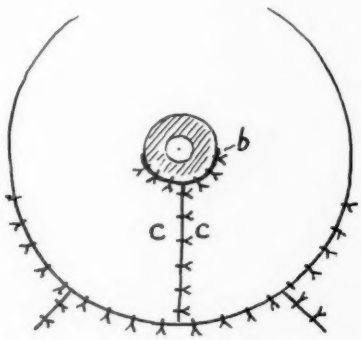
Fig. 3.

Fig. 2.—Area of retromammary excision (*a*), varying according to case but preserving central core of gland (*gl*) and subcutaneous blood vessels and fat. Posterior surface of breast bluntly separated along pectoral aponeurosis (*ap*) through incision in submammary fold (*s.m.*). (*f*) Skin flaps; (*m*) pectoral muscle.

Fig. 3.—Insertion of dermal loops (*1*, *2*, *3*) through posterior aspect of reduced breast and pectoral muscle (*m*). (a^1) Retromammary space following excision. (*s.m.*) Submammary fold; (*ap*) aponeurosis.



A.



B.

Fig. 4.—Skin plastic. *A*, Following incision along lower border of areola (*b*), midline and submammary fold, flaps (*c*, *c*) are mobilized. Excisions along midline and submammary fold (c^1, c^1).

B, After closure of flaps under areola (*b*) and along midline (*c*) and submammary fold.

The method described herein is not suitable when a greatly oversized areola requires circular excision. In such cases, mammectomy or the two-stage procedure of transposition[7] is indicated. However, a moderately wide areola can be safely reduced with this technique by excision along its lower border. Dissection in the areolar region must necessarily be superficial to preserve the periareolar venous and arterial plexuses.

SUMMARY AND CONCLUSIONS

1. The retromammary procedure described here affords a substitute for mammectomy with free grafting of the nipple (1) when the hypertrophy is mainly in the anteroposterior diameter and (2) when it is desired to preserve the sensitivity of the nipple. A greatly oversized areola is a contraindication.

2. The procedure consists of retromammary resections from the gland; the central segment, including the nipple, is preserved. This is followed by mastopexy by means of dermal loops and a double-flap skin plastic.

3. This method preserves the sensitivity of the nipple, which is lost or greatly reduced after mammectomy with free transplantation of the nipple.

4. Because of the absence of any interference with the main mammary vessels, the procedure can often be carried out safely in one stage.

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THE IMPLICATIONS OF LOCAL EXCISION OR SIMPLE MASTECTOMY PRIOR TO RADICAL MASTECTOMY FOR CARCINOMA OF THE BREAST

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A STUDY was made of 41 patients with proved carcinoma of the breast who had had simple mastectomy or local excision of the tumor prior to entering the Ellis Fischel State Cancer Hospital. The undesirable results which follow the use of simple mastectomy performed for diagnostic purposes or for any other reason prior to radical mastectomy are emphasized. The cases presented suggest that local excision followed by a delay of over two months may be detrimental to the ultimate welfare of the patient.

It has been the experience of others that poor surgical results are obtained from secondary radical operation after primary surgical excision or simple mastectomy in carcinoma of the breast. Adair[1] stated: "Of 283 cases classified as 'operable after local excision' there was a salvage of only 53 cases, representing 20 per cent. Had the patient been properly handled at the beginning, she at least would have had a 51 per cent chance of a 5 year cure." Harrington[2] reported in 1940 that 10 per cent of the patients with radical mastectomies done at the Mayo Clinic had had previous minor surgical procedures done elsewhere, and that 74 per cent of this group had lymphatic involvement, as compared with 63 per cent who had not had a previous operation.

Greenough[3] was of the opinion that exploration followed shortly by radical mastectomy diminishes little, if at all, a good prognosis in early carcinoma of the breast. He advised, however, that "delay between exploration and radical operation in cancer of the breast is to be avoided, and that exploration should not be done unless, and until, all arrangements for competent pathological examination by frozen section and immediate radical operation are available." In a series of 42 early cases with exploratory incisions, there were 53 per cent five-year cures. Siemens,[4] in comparing 59 cases in which biopsies were done with 260 cases with no biopsies, reported even better results in this group of 59, but emphasized that the good results were due to the fact that the lesions were noted earlier than in the 260 with no biopsies, that the tumor area was small, and the axillary metastases were limited. He showed that a better survival rate was maintained in these cases in spite of biopsy, and felt that biopsy in itself did not produce an untoward effect on the prognosis. Discussing these 59 cases in which biopsy was done at varying intervals, prior to operation, Siemens indicated that the prognosis was

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slightly worse when the interval between biopsy and operation was forty-five days or more as compared to delays of from one to 10 days.

It is generally conceded that biopsy of breast tumors in itself is not a dangerous procedure unless undue delay takes place between biopsy and subsequent radical operation. When a patient has a single lump in the breast, the tumor should be exposed in the operating room, and if there is any doubt as to the nature of the tissue, a frozen section should be done. Haagensen[7] has indicated that the procedure which least disturbs the tumor bed and which theoretically is the best is the incisional biopsy; this is especially true in the larger, more extensive tumors. It seems justified, however, when the suspicious single nodule is small (2 or 3 cm.) to remove it en bloc with a margin of healthy surrounding breast tissue. This gives the pathologist an opportunity to cut the entire nodule and do frozen sections as indicated. We have had several nodules in which carcinoma was present in only a small area which could easily have been missed by an incisional biopsy. With larger lesions excision en bloc is, of course, not practicable for frozen section; incisional biopsy should be performed when there is any doubt as to the nature of the process. The sharp scalpel rather than the cautery is recommended.

Simple mastectomy should not be used as a diagnostic procedure under any circumstances. Slaughter and Peterson[5] reported 13 patients who had had simple mastectomies for proved cancer, and all but 2 presented local recurrences when they were examined for the first time in the tumor clinic. Hicken[6] has shown that complete excision of mammary tissues is seldom accomplished in the usual simple mastectomy and that if the tumor is at all extensive, carcinoma is very likely to be left in the remaining breast parenchyma. Aspiration biopsy should also not be used as a diagnostic method in breast carcinoma (Haagensen[7]), for in this procedure the malignant area may be missed, or the material may be insufficient to distinguish architectural details and consequently unsatisfactory for accurate diagnosis.

Of the 41 cases in our group, 22 patients had radical mastectomies in our hospital (16 of these had had previous local excisions of the tumor, and 6 had had previous simple mastectomies) and the remaining 19 patients were considered to be inoperable on admission, and were given either palliative irradiation or no treatment at all. Of these 19 patients, 6 had had previous local excision and 13 had had previous simple mastectomy. Of the entire group of 41 cases, only 9 patients are living without disease and these had time intervals of two months or less between the primary procedure and radical mastectomy.

TABLE I. TWENTY-TWO PATIENTS RECEIVING RADICAL MASTECTOMY; TIME INTERVAL FROM FIRST TO SECOND TREATMENT

INTERVAL	NUMBER OF CASES
1 to 2 months	14 (all of the 9 patients living and well were in this group)
3 to 4 months	3
5 to 10 months	2
24 to 48 months	3

TABLE II. NINETEEN PATIENTS CONSIDERED INOPERABLE ON ADMISSION;* TIME INTERVAL FROM FIRST TREATMENT TO ADMISSION TO ELLIS FISCHEL STATE CANCER HOSPITAL

INTERVAL	NUMBER OF CASES
1 to 2 months	5
7 to 9 months	3
11 months	1
20 to 60 months	7
12 to 21 years	3

*All of these patients are now dead.

In the 19 patients in whom radical mastectomy was not done, the intervals of time from initial treatment to admission to our hospital were relatively longer, only 5 being admitted within two months following primary surgery.

Of the 12 patients who received radical mastectomy but are no longer living, 4 died within three to five months, and another 4 before twenty-two months had passed. In view of the fact that the patients not receiving subsequent radical mastectomy survived relatively greater lengths of time from initial treatment to death, we wonder if the patients' lives were not actually shortened by the second operation. Twelve of the 19 patients who were not given radical operation lived longer than thirty months. Six patients lived from eleven to twenty-one months, and only one died within a short period (two months). Of 11 patients receiving secondary radical mastectomy and subsequently dying from cancer, tumor was present in all of the operative specimens, in either the breast (1 case), axillary nodes (4 cases), or both (6 cases). The twelfth death was caused by a pulmonary embolus.

In the 22 patients who had radical mastectomy, there was considerable inaccuracy in the clinical examinations with regard to the presence of persistent tumor or axillary involvement. Errors (proved by pathologic examination of the specimen) were made in 12 (or 55 per cent) of the 22 cases, these mistakes usually made from not detecting the presence of actual axillary involvement. Other authors have quoted as high as 50 per cent error in this regard (Haagensen).

In 13 patients who had simple mastectomies prior to referral to our hospital, the radical operation was not carried out because they were considered inoperable upon arrival (see Table III). All of these patients have since died, 8 within one year of admission. Seven were given radiotherapy as a palliative measure, but life was not noticeably lengthened in these instances. It is interesting to observe the high incidence of local recurrences in this group as well as the presence of regional lymphatic involvement and distant metastases. Every case, with one exception, revealed evidence of at least one of these three phases of the disease and several cases exhibited all three.

In only 6 patients with previous simple mastectomies was it feasible to do radical mastectomy, and only 2 of these are now living without disease. Three died in relatively short periods following operation (2 lived two months, and 1 lived thirteen months). In the 2 living patients there was no evidence of axillary spread or persistent carcinoma in the surgical specimen, evidently demonstrating that the tumor was initially so small it was completely excised at the time of simple mastectomy. In the remaining 4 patients, all had evi-

TABLE III. PATIENTS WITH PREVIOUS SIMPLE MASTECTOMY; RADICAL MASTECTOMY NOT COMPLETED

AGE (YR.)	ONSET OF SYMPTOMS TO SIMPLE MASTECTOMY	TIME FROM SIMPLE MASTECTOMY TO E.F.S.C.H. ADMISSION	LOCAL RECURRENCE	AXILLARY NODES	OTHER METASTASES	TIME FROM SIMPLE MASTECTOMY TO DEATH	TIME FROM E.F.S.C.H. ADMISSION TO DEATH
67	1 mo.	48 mo.	0	+	Inguinal; pulmonary	68 mo.	19 mo.
50	9 mo.	7 mo.	+ Encuirasse	+ Bilateral	Supraclavicular	11 mo.	4 mo.
75	2 mo.	20 mo.	+ In scar	+	–	28 mo.	8 mo.
51	8 mo.	48 mo.	+ Mass	+	Axillary; skin nodules	60 mo.	12 mo.
72	6 mo.	16 yr.	+ Mass and skin nodules	0	–	19 yr.	3 yr.
39	6 mo.	8 mo.	+ Mass, bilateral	+ Bilateral	–	10 mo.	2 mo.
47	2 mo.	12 yr.	+ Mass	0	Pleural effusion	12 yr.	1 mo.
60	6 mo.	26 mo.	0	0	Supraclavicular	40 mo.	14 mo.
35	2 mo.	20 mo.	0	0	Inguinal; pulmonary	22 mo.	2 mo.
78	4 mo.	21 yr.	0	+	Axillary mass; skin nodules	22 yr.	12 mo.
67	36 mo.	11 mo.	+ Mass	+	Supraclavicular	13 mo.	2 mo.
66	2 mo.	2 mo.	0	0	–	66 mo.	64 mo.
69	4 mo.	36 mo.	+ Chest wall invasion	+	Cervical	56 mo.	20 mo.

dence of axillary involvement and 3 of these had local recurrences (with muscle invasion, etc.) as well. The final results in this group were notably poor even though the interval of time between simple and radical mastectomy was not unduly long: 4 with intervals of two months or less, and 2 with intervals of four and seven months, respectively. Fig. 1, the photomicrograph, illustrates the typical picture of local recurrence following simple mastectomy.

The 9 patients who are living without evidence of disease all had intervals of two months or less. This emphasizes the importance of the short interval between initial biopsy and radical treatment. The prognosis was uniformly good in spite of the fact that 3 of these patients had persistent tumor in the pathologic specimen at the site of previous excision. It is significant that the size of the removed tumors was uniformly small. Seven of these patients were previously treated by local excision, while the other 2 had previous simple mastectomies (see Table III).

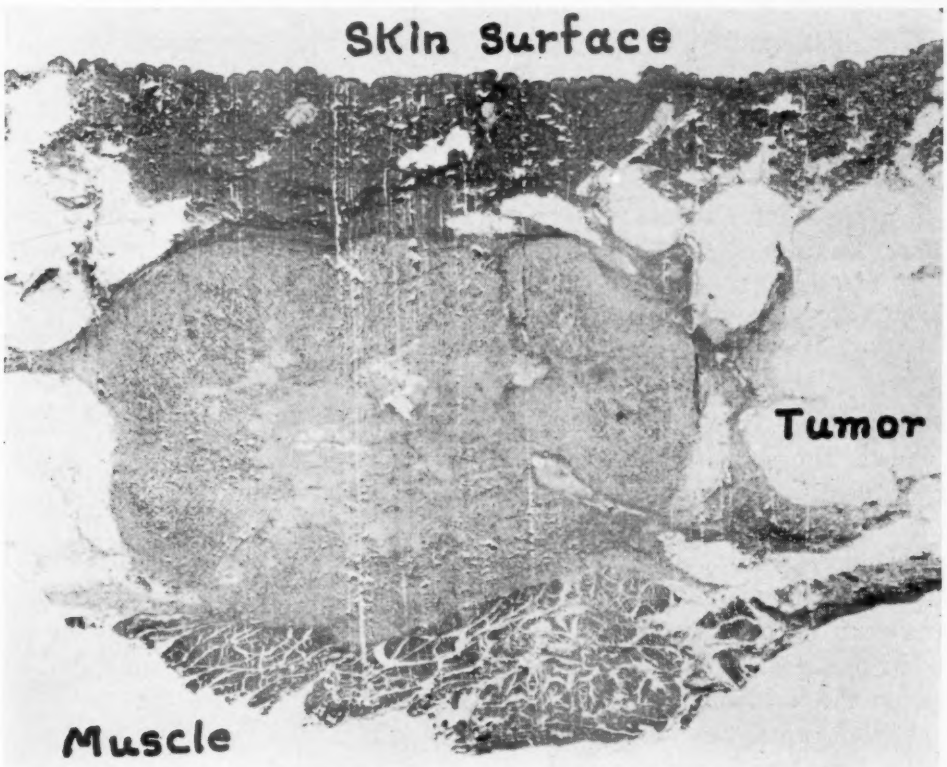

Fig. 1.—Persistent growing tumor following simple mastectomy. Carcinoma is directly invading pectoral fascia and muscle, and is present just beneath overlying skin (×3).

An additional 11 patients were found at Washington University who had radical mastectomy following simple mastectomy. Seven of these are now dead, and 4 are living with disease. There was a high percentage of local recurrence in this group and all are destined to die of cancer.

DISCUSSION

In our series of cases, noticeably better results were obtained in those patients wherein the delay from preliminary to final operation was not more

than two months. In fact, all of our 9 patients living without disease had intervals limited to that period. In the patients who had previous simple mastectomy, local recurrences frequently followed the subsequent radical operation. In the group of 13 patients with disease too far advanced for secondary radical operation, local and distant spread was a common finding. Furthermore, the interval of time from simple mastectomy to death in those 13 patients (all now dead) was far longer than in those who were submitted to secondary radical operation. We ask then, do radical operations performed after simple mastectomies actually hasten the death of the patient? A contributing factor in accounting for the prevalence of local recurrences following simple mastectomy might be the fact that in the performance of a simple mastectomy the amount of skin sacrificed is small, relatively thick skin and subcutaneous tissue flaps are usually dissected (often cutting across strands of tumor which reach upward toward the skin surface), and that these flaps are then plastered down against denuded pectoral fascia, providing an excellent bed for the growth of residual bits of tumor (Fig. 1). Also simple mastectomy is performed too often for larger tumors which are impossible to encompass by local excision. When radical mastectomy is performed for cancer following previous simple mastectomy, a far more extensive and difficult operation is required. All of the area which has been previously undermined in the raising of the flaps in the first operation must be removed widely en bloc, leaving a tremendous defect on the chest wall, which necessitates the use of extensive skin grafts. In fact, in our small group, radical mastectomy following simple mastectomy did not prolong the life of a single patient. In the 2 patients who survived, no tumor was found in the remaining breast or axilla so that apparently all the tumor was removed at the time of the first operation. These cases show that once simple mastectomy has been done for cancer, the prognosis is extremely poor in practically every instance. On rare occasions, however, the surgeon may be lucky enough to remove all the tumor with the simple mastectomy. In our group this fortuitous circumstance took place in only 2 out of 19 cases (9.5 per cent). The other 17 patients (91.5 per cent) are dead or dying. In spite of the fact that radical mastectomy following previous simple mastectomy did not change the prognosis in our group of patients, we still must reluctantly recommend it inasmuch as the subsequent radical operation may rarely cure the patient. In the case of the patient who demonstrates clinically local recurrence and/or regional lymph node metastasis it is questionable whether radical mastectomy is indicated. In this group of cases irradiation might give better palliation.

Diagnostically, simple mastectomy rarely provides more information than can be gained by simple biopsy of a tumor mass and, unfortunately, simple mastectomy occasionally introduces a temptation among some surgeons to temporize with the disease and to postpone further appropriate treatment.

Many human factors are responsible for the delay following biopsy which is so disastrous to the patient; and even though the intentions of the physician are the very best, he may be helpless in averting all extended postponement

of radical treatment. Patients, in general, dislike the idea of two separate operations and would much prefer to have their trouble handled "at one sitting," not only for economic reasons, but also in order to be relieved of the ordeal and associated anxiety. A patient's inertia with regard to his own welfare, even when urged by his doctor, is often a cumbersome influence. Also, in certain areas, admission to hospitals where radical operations can be performed may be hindered by waiting lists, or lack of bed space. Undesirable lapses of time should be avoided at all costs if possible.

CONCLUSIONS AND RECOMMENDATIONS

1. Biopsy of breast tumors should be done judiciously and with facilities for subsequent radical mastectomy immediately available.

2. If it is necessary to delay the radical procedure after local excision, the lapse of time before radical operation should be no longer than two months and certainly just as much sooner as is humanly possible.

3. Under no circumstance should simple mastectomy be employed as a diagnostic or therapeutic measure for an operable carcinoma of the breast. After such a procedure persistent carcinoma (as demonstrated by this series) almost invariably remains hidden in the operative field and/or axilla.

4. In 19 patients who had previous simple mastectomy in only 6 could radical mastectomy be completed and, of these, only 2 are living without disease. It is probable that in the patients who develop obvious local recurrence and/or regional lymph node metastasis after simple mastectomy, radical mastectomy is contraindicated. Irradiation as a palliative procedure would probably be of greater benefit in this group.

5. In 22 patients who had previous local excision, radical mastectomy was justified in 16 and, of these, 7 are living without disease.

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CANCER OF THE RECTUM

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THE cardinal objective in dealing with a cancerous lesion is to eradicate the disease process, and it is recognized that this can be achieved only by wide removal of the growth and all gland-bearing tissues. Methods designed solely for reasons of sentiment at the expense of survival of life should be deleted from our surgical armamentarium. Obviously, no surgeon of sound mind would deliberately or maliciously perform a procedure of limited scope for a resectable malignancy of the rectum if, by such procedure, recurrence would reasonably be expected to occur and the period of survival thereby curtailed.

The classical and popular type of extirpation is that devised by Miles—the method of abdominoperineal excision. I am frank to admit that if there were available but one operation for rectal cancer, my unqualified choice would be the Miles' procedure. Nearly twenty years devoted to bowel surgery have convinced me that any surgeon dealing with rectal and sigmoidal cancer in large numbers must have several methods at his disposal, methods not only with which he is acquainted but which he is capable of performing well. Our chief concern must be the individual patient; therefore, the commission of that common surgical sin of adapting the patient to the operation rather than the procedure to the patient should be avoided. Time upon time during the course of my experience, an alternate technique has been justified. While all of us today lean very decidedly toward single-stage resection, graded procedures must never be deleted entirely. The exteriorization method of Mikulicz and Rankin for sigmoidal growths, as well as colostomy and posterior excision (Lockhart-Mummery), and the two-stage Lahey-Cattell abdominoperineal excision for lesions of the anorectum have definite value in some instances. Owing to various factors intervening during the course of the operation, the seasoned operator may wisely select an alternate method. For these reasons, we are constrained to take issue with such a statement as, "There is only one operation for cancer of the rectum, namely, the Miles' procedure."

Contrary to common belief, we in our department do not condemn the Miles' procedure, evidence of which is the frequency of its performance in our department, but its use is confined to selected cases. On the other hand, we do not sanction a perineal colostomy in which the anal sphincters are sacrificed for the sole purpose of avoiding an abdominal stoma. We are emphatically critical of and unalterably opposed to the frequency with which an abdominal colostomy is established, not only by the occasional operator, but by those who are extirpating these growths in a large number of cases. Regrettably, the old axiom, "when in doubt do a colostomy" has not, but should

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be, relegated to the limbo of the forgotten past. It is common knowledge that a permanent abdominal colostomy is performed much too often, particularly in the presence of inoperable malignancy without obstruction. While not common knowledge, it is my honest contention that the establishment of an abdominal stoma and sacrifice of the sphincter musculature is needlessly instituted in a far greater percentage of cases than is indicated or required. These remarks should in no way be construed, nor has it been intended to imply, that the ideal solution has been achieved. But little has been contributed and possibly nothing of particular import, but like others, there is a striving for a method "par excellence" yet to be designed.

Interest, during the past several years, while centering around all phases of lower bowel malignancy, has dealt chiefly with the surgical management of malignant lesions in various segments of the lower bowel. Thus an opportunity has been afforded to investigate and re-evaluate the results, both immediate and remote, of methods employed to eliminate abdominal colostomy, particularly in the procedure advocated and popularized by Babcock in 1932.[1, 5] and in his subsequent publications.[2, 3, 4] This method, with which I have had some experience, is described under the term proctosigmoidectomy, but sometimes is referred to as the over-and-under or pull-through method.

Investigations in our department, while by no means exhaustive, have been directed toward various phases of the technique, but particularly toward the determination of the soundness and practicality of the procedure. For example, it was found that transplantation of the iliac sigmoid could be readily achieved anatomically and viability could be maintained by precise division of the sigmoidal vessels and preservation of the communicating arcades. This has been reported by Smith and the author.[6] It was observed that in a group of 146 consecutive cases, the average length of bowel removed by this operation was 29.6 cm., which is approximately the same amount as that excised by the Miles' method. Measurement at the point of arterial ligation averaged from 38 to 55 cm. from the coccyx tip, whereas, with the abdominoperineal method of excision, Gabriel recorded an average distance of 25 cm. It is recognized that the removal of an extended length of bowel is desirable because of the frequency with which additional lesions are encountered. Only last year, we[9] reported a series of 171 consecutive patients on whom an abdominoperineal proctosigmoidectomy had been performed for cancer. Fifty-four (31.2 per cent) presented a concomitant adenoma in the removed specimen; eleven (20 per cent) of these concomitant adenomas showed malignant degeneration.

Radicality implies extirpation of the cancerous bowel and wide removal of the gland-bearing areas. The chief concern was to determine the degree of radical extirpation obtainable by the method of proctosigmoidectomy. It was found that during the abdominal phase of the operation, all node-bearing tissue overlying the iliac vessels (upper mesocolic) could be readily mobilized for removal by a combination of sharp dissection and gentle separation as far as the bifurcation of the aorta. Included were those node-bearing areas throughout the mesosigmoid and around the superior hemorrhoidal vessels. Likewise, a wide expanse of mesorectum with its lower mesocolic nodes in

the sacral hollow, together with the glands of Gerota, could be separated easily and pushed forward by a single thrust of the hand distally as far as the coccyx tip. This maneuver would leave the sacral surface bare. The lateral ligaments were then divided widely as in any other procedure and mobilization was accomplished to the prostate in the male, or well into the rectovaginal septum in the female. No effort need be made to preserve the peritoneum for closure since no complete pelvic diaphragm is necessary. It was apparent that peritonization of uncovered surfaces and structures was unnecessary. In the perineal portion of the operation, wide removal of the levators could be effected as well as the major portion of the ischiorectal fat; also, it was found by precise dissection that the three bundles of the external sphincter and the internal sphincter could be preserved.

Those of us who are interested in this problem are familiar with the mode of spread well described by the investigations of various workers, such as Westhues, Dukes and Bussey, Coller and Kay, David and Gilchrist, as well as Glover and Waugh. Early in 1947 and recorded in 1948, we reported the findings in 146 consecutive cases, in which serial sections of the lower bowel specimens were made at 2, 4, and 6 cm. below the lower edge of the growth. In only one instance was malignancy disclosed at a distance of 6 cm. below the lower margin of the growth.

Elsewhere, we[11] have discussed the complications and sequelae peculiar to this operation and besides listing them in order of frequency, we have detailed various points in the technique and aftercare by which they may be avoided. Therein the statement was made that the complications in many respects were similar and approximately equal to those encountered by the Miles' operation. Such is true, but one must be mindful that our experience covered an eight-year period in which proctosigmoidectomy was performed on 434 patients, of which 401 operations were for cancer. Suffice it to declare, there are many pitfalls into which even the most expert technicians may fall.

Adequate mobilization, viability of transplanted bowel, wide removal of the gut with node-bearing areas, and obstruction due to pelvic descent of small intestine have not been the chief concern. The problem, in the main, has been in regard to anal sphincter continence. While some of the surgeons who have attempted this procedure have maintained but meager continence, by meticulous dissection it has been possible to preserve the three bundles of the external sphincter and also the internal sphincter muscles. Certainly, some degree of injury occurs by reason of traction and trauma. It may be mentioned that Jerome Wagner of New York has demonstrated the somatic innervation to be intact macroscopically and microscopically with this procedure. Filaments from Meissner's plexus to the internal sphincter must of necessity be severed, although, as has been described, sympathetic fibers are present with the cerebrospinal chain.

It may be recalled that Babcock[12] advocated posterior division of the anal sphincter musculature solely for the purpose of preventing necrosis of

the protruding bowel by the too active contractions of this muscle, a step to which we do not adhere. The patients do not wear pads, do not soil themselves during waking or sleeping hours, and are not placed on a restricted diet except in the immediate convalescent period and then only when they imbibe fruit juices. Even though an urge for stool is experienced, whereupon the patient contracts the anal sphincter muscles voluntarily and voluntarily empties the bowel in a leisurely period of from fifteen to thirty minutes, the degree of continence is not as complete as that in the normal individual or with the group wherein low anastomosis is performed.

Wangensteen[13] has mentioned that from his experience with the abdomino-anal pull-through procedure, "the healing phase is longer and it is wise to make a complemental diversionary colostomy to afford rest to the pelvic colon pulled through the remaining distal sphincteric segment." I must take issue with this conclusion, because in this series of rectal cancer there is but one instance in which a proximal stoma was instituted and, in this case, a cecostomy was made prior to proctosigmoidectomy, solely to evaluate the rationality of decompression by inserting a Miller-Abbott tube through the stoma. As for healing time following proctosigmoidectomy, approximately three weeks is required. As mentioned previously,[14] our patients are out of bed usually on the fifth, or even the fourth day, are discharged from the hospital on the tenth postoperative day, and the majority return to work in from four to ten weeks following the operation. The mortality rate with this procedure is 4.9 per cent; the five-year survival rate, including those for palliation as well as for cure, is 52.6 per cent, and the incidence of local recurrence in patients on whom proctosigmoidectomy have been performed for five or more years is 17.9 per cent[15] in spite of a resectability rate of 87.7 per cent.

During this discussion, experience with one method employed to eliminate an abdominal colostomy has been emphasized, but the remarks herein contained must not be construed to mean that this procedure is recommended as a routine measure, or for all cancerous lesions located in the anus, rectum and pelvic flexure. Lest misunderstanding be invoked, may I digress and cite what has been, in general, the method of approach to the surgical management of malignancy in the lower segment of the bowel.

1. All growths involving the mid- and proximal sigmoid are removed by (a) immediate establishment of intestinal continuity, either by open or closed technique, or (b) the Mikulicz-Rankin method of exteriorization.

2. All lesions involving the distal sigmoid, rectosigmoidal, and ampullary rectum are extirpated by proctosigmoidectomy without colostomy and with preservation of both the internal and external sphincters.

3. Those lesions involving the anal canal and lowest 3 cm. of the rectum are excised by the method of Miles—the abdominoperineal excision.

During the eight-year period ending with this Honolulu meeting, there were in my files the records of exactly 800 patients with malignancy of the anus, rectum, and sigmoid colon. It will be noted that some type of abdominoperineal excision was instituted in 145 cases, and abdominoperineal procto-

sigmoidectomy without colostomy and with preservation of the sphincter musculature was performed on 401 cases.

TABLE I. AUTHOR'S SERIES, TABLE OF THE PROCEDURES

PROCEDURE	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
1. Sigmoidectomy (end-to-end anastomosis Mikulicz-Rankin, Hartmann)	90	8	8.8
2. Abdominoperineal proctosigmoidectomy	401	20	4.9
3. Abdominoperineal excision (Miles, Lahey, Lockhart-Mummery)	145	5	2.7
4. Perineal resection (Cuneo-Seneque)	2	0	0
Total	638	33	5.1

SUMMARY

A personal series of 800 patients with malignancy of the lower bowel on whom radical resection was performed in 638 instances serves as a basis for comment. Excision by the abdominoperineal method with the establishment of a permanent abdominal stoma, preferably by the method of Miles, is recommended for all growths involving the anal canal and lowest 3 cm. of the rectum, and very definitely no attempt should be made to preserve the sphincter musculature for lesions in this area. Cancerous processes cephalad to this site may be removed by the procedure designated by Miles, although our preference is proctosigmoidectomy. Those who manifest interest and wish to master the technique of proctosigmoidectomy will find it a method suitable for ampullary growths of the rectum, the rectosigmoid, and the terminal pelvic colon. An experience of eight years, during which period this method was employed in a group of 401 patients with cancer, provides evidence that the operative mortality rate is low, the period of morbidity diminished, and the five-year rate of survival parallels, and in some instances, is better than that obtained by the Miles and other procedures. The incidence of local recurrence is greater by less than 2 per cent, using the exhaustive investigations of Gilchrist for comparison; sexual impotence in the male is decreased and anal sphincter function is satisfactorily uniform. If and when the statistics evidence the fact that the results in a larger group of patients than is now available, and particularly the ten-year rate of survival, do not compare favorably with those achieved by other methods, then shall the error be acknowledged and the procedure completely deleted from the surgical armamentarium.

As Wangensteen has aptly stated, "we cannot resolve our differences by debate but rather by analyzing our experiences critically and recording them truthfully. Time is the final arbiter of all things. Until she has given her answer let us be tolerant of our honest differences of opinion."

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PRINCIPLES AFFECTING SUCCESSFUL ESOPHAGEAL ANASTOMOSIS

A Report of Twenty-Three Operations, Without Operative Mortality

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THE time is apparently at hand when resections and anastomoses involving the esophagus are as safe as those associated with any other organ. As recently as June, 1948, published hospital mortalities for such operations were generally in the neighborhood of 30 to 35 per cent. There seems little reason to doubt that present methods will improve even further. Textbooks cannot keep pace with the many improvements and advances which have made possible vastly better operative techniques and end results. From the early days when subtotal gastrectomy was performed with mortalities ranging from 50 to 75 per cent in the best of hands to the present day, when the occasional death from the operation is the result of factors presently not under the control of the surgeon, has been a relatively short time. The gradual standardization of surgical techniques and training, advances in anesthesiology, and the science of nutrition have all played their part in the accomplishments of this present day. Yet it is not at all unlikely that operative deaths, which today we consider as beyond the realm of surgical and medical control, will at some future time be prevented with the same ease as the once feared pulmonary atelectasis. To digress from the gastrointestinal field for a moment, the present successful revival of the Wertheim operation for cancers of the uterus is an excellent illustration in point.

Although the successful adoption of many of our surgical techniques has required many years, the really astounding improvements in operative mortalities after esophageal anastomosis have been brought about in less than ten years. For during this short period of time, the operations of total gastrectomy, resection of the gastric cardia, and esophagectomy have become standardized. Pack and McNeer reviewed the literature of all published total gastrectomies in 1943, including twenty cases of their own, and found an operative mortality averaging well over 33⅓ per cent under the best of circumstances. The causes of death were in the main the result of peritonitis, bronchopneumonia, and heart failure. Since post-mortem examinations were not granted in all instances, the exact state of the esophageal anastomosis could not always be determined. The significant fact remains, however, that when an autopsy was performed, peritonitis was all too often encountered. Likewise fistulas occurred in a high percentage of cases (30 to 40 per cent). Interestingly enough, we have all been made aware of the change in physical findings in peritonitis resulting from chemotherapy and antibiotic agents.

Numerous operative techniques were devised to protect, buttress, and support the esophageal anastomosis with jejunum or stomach both above and

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below the diaphragm. Roscoe Graham went so far as actually to obstruct the jejunal lumen in this attempt, though providing an adequate by-passing of duodenal contents. Yet his mortality records demonstrated no obvious improvement.

The historical evolution of these operations has been thoroughly discussed in previous publications. Except for the supra-aortic esophagogastrostomy, they had all been attempted on numerous occasions by Sauerbruch, Wendel, etc. Unquestionably the real credit for their successful adoption must go to Garlock, Pack, and Sweet, who have standardized these procedures and made them safe and feasible. Garlock not only revived this field of surgery, but extended the operation of esophagogastrostomy to resection of esophageal cancers above the aortic arch. The gradual adoption of Sweet's technique of esophageal anastomosis has been one of the most important factors in the successful performance of esophagogastrostomy, for there is no other procedure which demands such meticulous attention to every detail at each stage of a long surgical seance. Frequently after a fatiguing, tedious dissection of the tumor, the operator would welcome the completion of the operation by another surgeon. Yet the care with which the anastomosis is constructed determines the success of the entire procedure. There can be little question that a fall in medical complications invariably follows the attainment of a sound surgical technique. Conversely, there is probably no other group of procedures of which it may be said with greater truth, that the operation is merely an incident in the management of the disease.

Preoperative Care.—Factors governing the correction of the starvation state which all too frequently affect these patients have been widely and repeatedly elaborated in surgical and medical literature. An intelligent application of the principles of establishing a positive nitrogen balance wherever possible, the restoration of electrolytes, water balance, and vitamin replacement, is taken for granted. It has not been necessary to perform jejunostomy preoperatively in a single instance; in fact, we doubt if the occasion need arise at all. It should be avoided at all cost, as the jejunum may well be required in the anastomosis. An estimation of the vital capacity, an electrocardiogram, a film of the lungs, and a urine concentration test comprise the list of special examinations preoperatively. Regardless of all the recent studies in the use of protein substitutes, let it be said here and now that in my opinion there is no substitute for blood transfusion in the pre- and postoperative phase as well as during the operation itself.

Operative Technique.—The patient is placed either in the supine or right lateral decubitus position depending on whether the procedure is to be performed above or below the diaphragm. Where the possibility of laparothoracotomy is entertained, slight elevation of the left hemithorax up to forty-five degrees is advisable. After one year's experience with laparothoracotomy for cancers of the gastric cardia, the incision was limited to the performance of total gastrectomy where additional exposure might be advisable. Though the exposure so obtained may well be superior to thoracotomy alone, it is not

so greatly enhanced as to make up for the additional surgical shock and extended operative time required for wound closure.

A fact that is not adequately appreciated by most abdominal surgeons of even great experience is that far greater surgical shock attends operations in the upper abdomen via laparotomy and especially laparothoracotomy as opposed to thoracotomy. The smoothness of the postoperative phase, with particular regard to intestinal stasis, is incomparably superior after thoracotomy. If the lesion is in the region of the diaphragm there is no need or excuse for laparotomy. As Sweet has pointed out time and again in his communications, there can be no possible advantage in approaching either carcinoma, diverticulum, ulcer, or hernia in this region by any other route. As he stated most aptly, it would be "analogous to attempt to repair a large inguinal hernia through a laparotomy incision." The needless fear of thoracotomy held by most general surgeons impels them to employ laparotomy. The successful management of the spleen through the open thorax is especially gratifying.

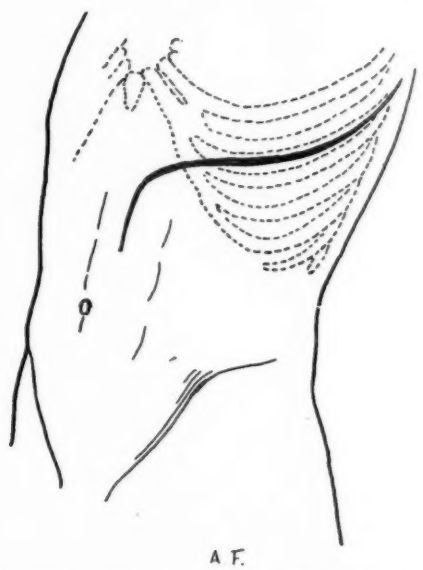

Fig. 1.—Incision for laparothoracotomy. (From Pack and McNeer, SURGERY, 1948.)

It is believed that resection of a rib rather than intercostal spreading and fracture is preferable because exposure is superior, the wound closes more easily and is less painful postoperatively.

Since appreciating the remarkable advantage of laparothoracotomy for total gastrectomy, all patients undergoing gastric operations for cancer are preferably anesthetized by intratracheal ether. It is never possible to tell from studies of x-ray films how high a resection may be required. Hence, when performing gastrectomy for cancer, spinal anesthesia is not advised. It is very comforting to know that the incision may be extended into the thorax when necessary. Clamps are never to be placed across that part of esophagus subsequently to be used in the anastomosis.

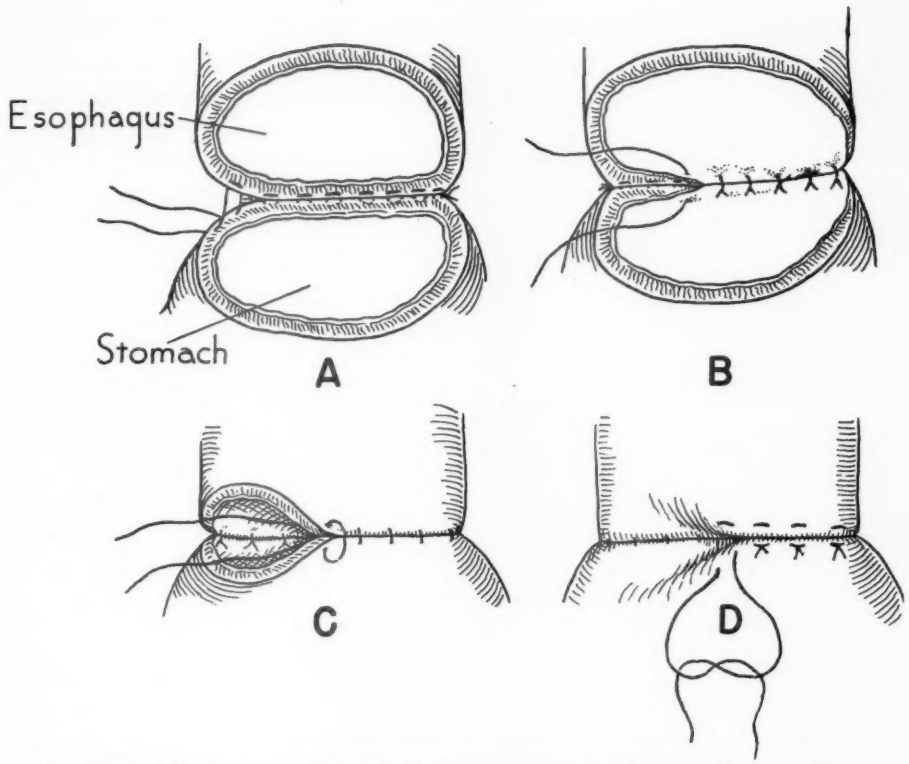

Fig. 2.—Technique of anastomosis between esophagus and stomach or jejunum. *A*, First layer of interrupted mattress sutures of fine silk uniting outer layers of the two organs; *B*, interrupted sutures through all layers, carefully apposing mucosal surfaces; *C*, same as in *B*, inverting the anterior layer; *D*, closure of outer layer anteriorly with interrupted silk.

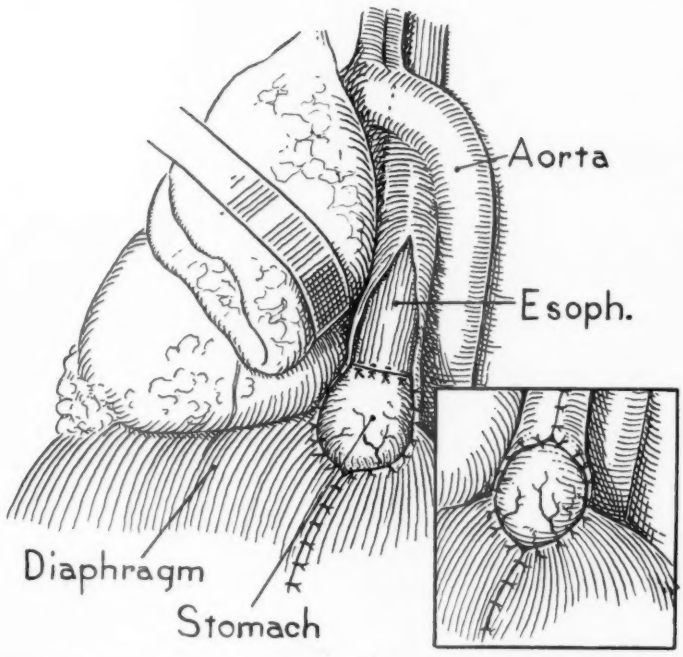

Fig. 3.—Esophagogastrostomy after resection of the gastric cardia; suture of operative site to mediastinal pleura.

Regardless of whether esophagus is anastomosed to stomach or jejunum, the adoption of an interrupted nonabsorbable suture in two or three layers as advocated by Sweet is absolutely fundamental to the success of the procedure. Meticulous apposition of the mucosal surfaces must be observed in

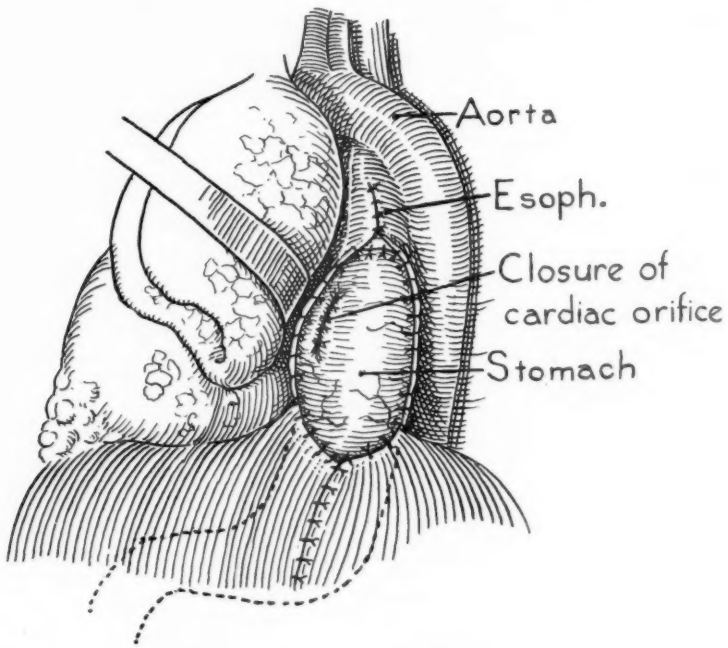

Fig. 4.—Esophagogastrostomy after resection of the mid-esophagus.

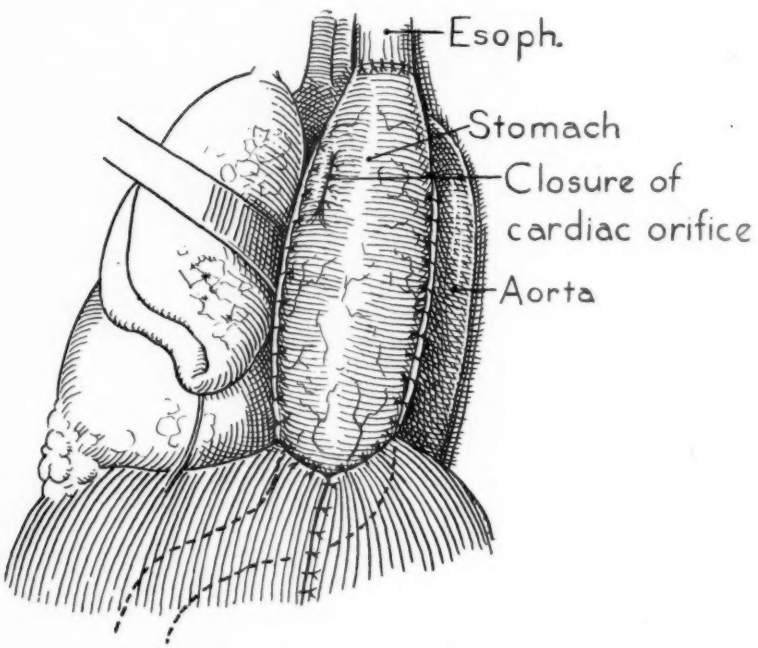

Fig. 5.—Supra-aortic esophagogastrostomy.

order to prevent subsequent stricture. A continuous inner layer of catgut tends to act as a purse string and thus obstructs the lumen. Though the employment of an interrupted fine silk technique may be time consuming, the results justify it in the long run. A definite point is made to insert sutures at right angles to the esophageal musculature always in through-and-through fashion. The integrity of the anastomosis depends on this principle more than any other. If, in addition, the esophagus is not dissected enough proximally to require ligature of any of the vessels supplying it with blood, there should be no concern regarding its integrity.

Retraction of the wound edges is vital if adequate exposure is to be obtained, yet it must be cautiously employed. Frequently in the past the retractors have been applied in too close approximation to the heart, particularly if the diaphragm has not been opened, during total gastrectomy. Serious cardiac changes have been observed which tended to compromise both the operative and postoperative phase. Since recognizing this danger, the retractors are never placed in such a position that they may forcefully compress the heart either above or below the diaphragm. The lessening of unfavorable cardiac reflexes and the tendency toward shock have been especially gratifying.

Fixation of the anastomosis to adjacent structures promotes wound healing by immobilization of the operative site. The infradiaphragmatic anastomosis must be sutured to diaphragm, hepatic ligament, or left lobe of liver depending on which is closest to the suture line. When constructed within the thorax the entire segment of stomach or intestine must be carefully sutured to diaphragm and preaortic pleura. In this way, the entire anastomosis is in fact buried in the mediastinum.

We have observed that since the underwater drainage tube has been placed just within the thorax and not down close to the anastomosis, the occurrence of fistula has ceased.

Postoperative Care.—Though the trachea has been aspirated at the termination of the operation and the lungs frequently re-expanded, the tendency to postoperative pulmonary atelectasis is still great. The most important single contribution toward the lessening of serious postoperative pulmonary complications has been the frequent aspiration of the trachea by the house staff. This is performed on the evening of the operation and twice daily thereafter until the patient is capable of raising the sputum himself. In addition, blow bottles, carbogen, early rising, and intramuscular injections of penicillin are employed prophylactically. Since ligating the superficial femoral veins preoperatively, pulmonary embolus has not occurred.

Too great emphasis cannot be placed on the value of postoperative tracheal aspiration. Since its adoption in all instances of high gastric and esophageal resections, there have been very few serious pulmonary complications.

Indwelling Pharyngeal Tubes.—The use of indwelling nasal tubes for feeding purposes is greatly to be deplored. The tendency toward fatal pulmonary

TABLE I. ESOPHAGEAL ANASTOMOSES, SUMMARY OF CASE HISTORIES

CASE	PATIENT AND AGE	OPERATION	DIAGNOSIS	COMPLICATIONS	END RESULT
1	R. P. 51	Esophagectomy and esophagogastrostomy 5/4/47	Epidermoid carcinoma of esophagus with lymph node metastasis	None	Died of metastasis, 6/24/47
2	S. L. 68	Abdominothoracic total gastrectomy and esophagojejunostomy, 5/27/47	Adenocarcinoma of stomach with lymph node metastasis	None	Died of metastasis, 11/17/47 (6 mo.)
3	L. M. 55	Abdominal resection of gastric cardia and esophagogastrostomy, 6/20/47	Adenocarcinoma of stomach with lymph node metastasis	Transient tachycardia	Died December, 1947 (6 mo.)
4	S. D. 45	Transthoracic resection of gastric cardia and esophagogastrostomy, 8/5/47	Colloid carcinoma of stomach	Pulmonary atelectasis	Died 8/5/47 (3 mo.)
5	A. D. 38	Transabdominal total gastrectomy and esophagojejunostomy, 8/12/47	Adenocarcinoma of stomach with lymph node metastasis	None	Living with metastasis (8 mo.)
6	C. R. 59	Transthoracic resection of gastric cardia and distal esophagogastrostomy, 9/16/47	Peptic ulcer	None	Living and well
7	A. Z. 58	Abdominothoracic total gastrectomy and esophagogastrostomy, 10/9/47	Adenocarcinoma of stomach with lymph node metastasis	Atelectasis, bronchopneumonia	Living and well
8	D. 59	Transthoracic total gastrectomy and esophagojejunostomy, 12/2/47	Gelatinous adenocarcinoma of stomach with esophageal extension	Pleural effusion	Operative survivor; cancer found at line of resection
9	D. 59	Transthoracic esophagectomy and jejunectomy and esophagojejunostomy, 1/6/48	Same	None	Living and well (5 mo.)
10	F. Z. 52	Abdominal total gastrectomy and esophagojejunostomy, 12/13/47	Colloid carcinoma of stomach with lymph node metastasis	Intestinal obstruction requiring laparotomy	Living and well (5 mo.)
11	A. B. 55	Transthoracic resection of gastric cardia and esophagogastrostomy, 12/10/47	Adenocarcinoma of stomach, Grade II, with lymph node metastasis	None	Living and well
12	V. M. 35	Transthoracic esophagogastrostomy, 1/8/48	Cardiospasm	None	Living and well
13	M. M. 51	Transthoracic total gastrectomy and esophagojejunostomy, 3/9/48	Adenocarcinoma of stomach, Grade II, with lymph node metastasis	Pleural effusion	Operative survivor; laparotomy for obstruction due to recurrence 5/18/48
14	F. K. 34	Abdominal resection of recurrent gastric tumor and esophagojejunostomy, 3/16/48	Lymphosarcoma (1941); gelatinous adenocarcinoma (1948)	Pleural effusion	Living and well (unusual sequence of gastric tumor)

TABLE I--CONT'D

CASE	PATIENT AND AGE	OPERATION	DIAGNOSIS	COMPLICATIONS	END RESULT
15	S. 65	Transthoracic resection of gastric cardia and esophagogastrostomy, 3/25/48	Adenocarcinoma of stomach, Grade II, with lymph node metastasis	None	Living and well
16	C. L. 36	Abdominothoracic total gastrectomy and esophagojejunostomy, 4/2/48	Gelatinous adenocarcinoma of stomach	None	Living and well
17	C. S. 57	Esophagectomy and esophagogastrostomy, 4/27/48	Epidermoid carcinoma of esophagus with metastasis to liver	None	Living and well
18	M. D. 59	Transabdominal resection of the gastric cardia, esophagogastrostomy and gastroenterostomy, 6/22/48	Peptic ulcer	None	Discharged
19	J. M. 49	Transthoracic resection of the gastric cardia and esophagogastrostomy, 6/12/48	Adenocarcinoma of stomach, Grade III, infiltrating gastric wall, metastases to lymph nodes	Pleural effusion	Discharged
20	J. S. 54	Transthoracic total gastrectomy, esophagojejunostomy and jejunojejunostomy, 6/22/48	Adenocarcinoma of stomach with lymph node metastasis	None	Discharged
21	A. W. 69	Transabdominal total gastrectomy, esophagojejunostomy and jejunojejunostomy, 7/1/48	Adenocarcinoma of stomach with lymph node metastasis	None	Discharged
22	J. E. 61	Esophagectomy and esophagogastrostomy, 7/20/48	Epidermoid carcinoma of esophagus with metastasis to right cervical lymph node	None	Discharged on full diet
23	P. B. 71	Esophagectomy and esophagogastrostomy, 8/5/48	Leiomyosarcoma of esophagus	None	Discharged on full diet

TABLE II. OPERATIVE PROCEDURES INVOLVING ESOPHAGEAL ANASTOMOSES

1. Total gastrectomy and esophagojejunostomy for cancer of the stomach	9
2. Resection of gastric cardia and esophagogastrostomy { for cancer	5
{ for ulcer	2
3. Esophagectomy and esophagogastrostomy for cancer of the esophagus	4
4. Resection and esophagojejunostomy for recurrent esophageal cancer	1
5. Resection and esophagojejunostomy for recurrent gastric cancer	1
6. Esophagogastrostomy for benign cardiospasm	1
Total number of operations	23

complication thereby has been demonstrated conclusively. In addition, the patient is made just that much more uncomfortable. When one sees the slime and filthy debris clinging to an indwelling tube after one week's intrapharyngeal residence, one cannot help but be impressed with the higher frequency of pneumonia attendant on its use.

Oral Feeding.—Of possibly still greater importance is rejection of the heresy which has governed the optimum time for feeding these patients. As soon as peristalsis is heard in the abdomen (twenty-four to forty-eight hours), the patient is given water and tea by mouth. Clear liquids are given as tolerated in ever-increasing amounts, so that by the seventh to tenth day the patient ingests a soft diet. This method has numerous advantages. First of all, the patient is delighted and encouraged beyond imagination. Second, the saliva produced in large amounts daily is diluted and cannot so readily cling to the edematous borders of the anastomosis. Third, the necessity for continuing parenteral fluids rapidly decreases so that by the fifth day all feeding is by mouth, as a rule. The tendency toward intolerance of parenteral fluids in large amounts by elderly subjects has strengthened the attitude in regard to limiting parenteral fluids. It was observed that these subjects often tolerate 2000 c.c. of glucose and water daily, more readily than the 3000 to 3500 c.c. as previously employed. There is far less tendency toward circulatory failure if such patients have a daily urinary output of 1000 c.c. rather than 2000 c.c. What is probably equally important is that the urinary specific gravity more nearly approaches normal as a result, thus indicating an improved water balance. Most interesting of all is that these individuals have usually regained their preoperative weight by the fourteenth postoperative day and are ready to go home—at a time when most surgeons are just beginning to permit them oral feedings.

Formerly, an auxiliary jejunostomy was constructed for feeding purposes. This has been abandoned as a result of the good effects of early oral feeding. The high frequency of diarrhea and occasional intestinal obstruction have likewise militated against jejunostomy.

There seems to be no indication in any of these patients adequately prepared for operation that hydrolyzed protein feedings in the postoperative phase offered any material assistance. In fact, the tendency toward bloating, fulness, nausea, and diarrhea was greatly enhanced. Transfusion of whole blood and supplementary oral feedings of a diet high in protein were far more efficacious.

Material.—The case histories of twenty-two patients upon whom were performed twenty-three consecutive anastomoses involving the esophagus without hospital mortality form the basis of this study (Table I). Fistula did not occur in a single instance. Stricture of the anastomotic site occurred on five occasions, the result of recurrent cancer in all instances, permitting reoperation and successful resection in one.[13, 14] In Case 19, a 34-year-old patient had undergone subtotal resection in 1941 for a gastric lymphosarcoma. Recurrence in the operative incision required protracted high voltage x-ray

therapy in 1942. In 1948 symptoms denoting obstruction at the gastroenterostomy demanded laparotomy, at which time the remaining stomach, upper jejunum, and transverse colon were resected and the appropriate anastomoses constructed. Pathologic study of the resected specimen revealed gelatinous adenocarcinoma of the gastric remnant invading the stoma of the gastrojejunostomy and the transverse colon. No explanation of this astounding pathologic entity has been offered by the pathologist. Sixteen patients underwent resection for adenocarcinoma of the stomach; four for epidermoid cancers of the esophagus; one for leiomyosarcoma of the esophagus; and two for benign gastric ulcer. Esophagogastrostomy was performed for refractory cardiospasm in one instance (Table II). Interestingly enough, two total gastrectomies for carcinoma were performed on men in their mid-thirties for lesions suspected preoperatively, both clinically and radiographically, of being benign gastric ulcers. Likewise, resection of the cardia was carried out on one individual for an enormous ulceration of the cardia involving spleen, tail of pancreas, diaphragm, and left lobe of liver, which proved to be peptic in origin. Esophagectomy was performed on one patient (Case 22) in spite of the presence of a metastasis to the liver, and in another patient in the face of a metastasis to a cervical lymph node. It was thought that they might thereby be offered far more palliation than by gastrostomy. Two weeks postoperatively they were enjoying a regular diet. The resection of readily mobile obstructing cancers of the esophagus in the presence of distant metastases must therefore be placed on a basis comparable to the management of similar lesions elsewhere in the gastrointestinal tract.

All patients are carefully studied fluoroscopically after barium swallowing and a few x-ray films made of the anastomotic site, prior to discharge from the hospital. This study affords a valuable comparison for the future in the event that stenosis does occur.

Our short experience with secondary operations for recurrent gastric and esophageal cancer thus far suggests that such lesions may be successfully resected more often than we realize.

Pulmonary complications were remarkably infrequent and mild as a result of the measures suggested in this communication.

RESULTS

This study covers a period of slightly over one year and hence results may not properly be evaluated. Undoubtedly some of these patients will remain well. Some have already died and others will likewise do so.

In the absence of distant metastases, there is no known method by which the operating surgeon may differentiate between the patient who will soon die of recurrence and the long-term survivor. Hence, all operable lesions must be resected. It is peculiarly pertinent to observe one patient (Case 13) who, having undergone transthoracic-total gastric resection, was found to have carcinoma infiltrating the proximal line of resection. Esophageal obstruction soon intervened, requiring thoracotomy a second time. When cancer was found to invade the anastomosis, it was resected en bloc and esophagus re-

anastomosed to a jejunal loop. The successful conclusion of this procedure has greatly altered our point of view regarding recurrent gastric and esophageal cancer and brought forward two suggestions:

1. Always resect for recurrent cancer if no distant metastases are demonstrable.
2. Submit the proximal portion of all esophageal resections to frozen section, delaying anastomosis until pathologic study has been completed.

An interesting fact is that six of these operations have been conducted at a relatively small county hospital for the first time. The success gained in their performance has been the direct result of the inescapable conclusion—that these operations can be performed in any good hospital provided that, in addition to the surgeon, there is provided good anesthesia, good nursing, and the intelligent follow-up care of a well-trained resident surgeon. Constant vigilance and meticulous attention to the innumerable minutiae of postoperative management are invariable requirements at all times. There is no doubt but that these procedures will be performed with ever-increasing frequency in smaller institutions as these conditions obtain more widely.

SUMMARY AND CONCLUSIONS

1. Experiences with twenty-three consecutive esophageal anastomoses without hospital mortality are recorded.

2. Principles regarding the minutiae of postoperative care are stressed.

3. Early oral feeding is advised.

4. Exploration of recurrent gastric and esophageal cancer is suggested.

5. Resection rather than gastrostomy as a palliative procedure is proposed for readily mobile obstructing esophageal cancers associated with distant metastasis.

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TRAUMATIC ILIAC HERNIA WITH EXTENSIVE SOFT TISSUE LOSS

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HERNIAS through natural foramina of the pelvis, such as sciatic and obturator, have been repeatedly described. However, herniation of the intestines through an artificial aperture in the iliac wing as a sequel to a comminuted fracture has not attracted much attention in the voluminous literature on hernia.

Extensive comminution of the ilium leading to the development of a permanent and substantial defect is quite unusual, but does occur, particularly in military traumatology as a result of destruction due to gunshot wounds. Such bony defects represent potential channels for herniation of the pelvic content. Ordinarily the powerful muscular mass overlying the ilium offers additional protection. If this soft tissue pad is also destroyed, a herniation of the intestines is an obvious sequel. When the defect involves the left ilium the nearest intestinal segment is the descending colon or its portion, often described as iliac colon.*

As a rule, the mobility of the descending colon is limited by its attachment to the peritoneum. However, in 36 per cent of cases (according to Treves) the descending colon has a well-developed mesocolon. In such an instance, when an opening in the pelvic wall exists adjacent to the colon, the intra-abdominal pressure will force a fragment of the colon out of the pelvic cavity as much as the length of the mesocolon will permit, and a hernia will result.

Oldfield described a case of a cecal hernia through a defect in the right ilium which developed after quarrying bone grafts from it repeatedly. The surrounding soft tissues were essentially intact, except for the surgical trauma.

The two most important principles of any herniorraphy are: first, elimination of any "niche" on the internal surface; second, utilization of dynamic structures. The pressure of an intra-abdominal organ will act like a wedge against a depression in the abdominal wall and ultimately weaken the outer structures. Inactive tissue alone, such as fascia, is unreliable for permanent repair. A satisfactory closure should include a dynamic blockade of muscle, or fascia held tense by muscle, preferably forming the internal wall. Obliteration of a large defect in the iliac wing can best be done by utilizing adjacent soft tissues, muscle, periosteum, etc., if sufficient material is available locally to accomplish a multi-layer suture. If this is not the case, the closure may be

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*The descending colon extends down to the superior aperture of the lesser pelvis where it joins the sigmoid. The lower portion of descending colon below the iliac brim is also known as the iliac colon.

attempted by using a large sheet of fascia lata, tantalum mesh or plate, or a bone graft. The presence of intact skin and subcutaneous tissue is an essential requirement for any successful closure of a bony defect, whatever, the procedure. If the surrounding soft tissue is lost and the skin is scarred or replaced by free skin grafts, resurfacing with a thick skin flap must precede any attempt to close the defect. The flap should not be limited to the size of the bony aperture, but should extend beyond it on all sides.

The case described here presented extensive destruction of both bone and soft tissues and offered a combined problem of resurfacing and obliteration of a large opening in the ilium.

Fig. 1.—Condition on admission; note bulging hernia.

Fig. 2.—X-ray views after barium enema showing the "double barreled" hernia of iliac colon.

CASE REPORT

A 31-year-old soldier was injured by a fragment of mortar shell in action in France on July 31, 1944. He suffered a compound comminuted fracture of the left iliac wing with extensive loss of soft tissues in the left flank. He was treated at various places along the chain of evacuation and on Aug. 29, 1944, while in a numbered General Hospital overseas, an attempt was made to resurface the soft tissue defect with contiguous flaps. However, because of a partial necrosis of a delayed flap, this plan was abandoned and the wound covered with a temporary split graft. In October, 1944, he was evacuated to the United States. On Feb. 10, 1945, he was admitted to Cushing General Hospital.

Examination on admission revealed a short, stocky, rather obese patient with an extensive defect, 10 by 8 inches, in the left flank along the posterior crest of the iliac bone and over the sacrum (Fig. 1). The loss involved skin, subcutaneous and muscular structures. The area was covered with a scar and thin skin grafts which, for the most part, were adherent to the underlying bone. Posterior to the anterior iliac spine there was a defect in the ilium admitting a thumb. Protruding from this defect was a thin-walled hernial sac which spread to a bulge of 3½ inches in diameter. The sac was covered with a thin skin graft. The hernia bulged on coughing and was easily reducible. Pressure on the hernial sac gave the patient a sensation of desiring to defecate.

A triangular flap 3 inches wide at its tip was outlined along the upper border of the scarred area. Originally it extended almost to the spine, but its distal 4 inches had sloughed and were replaced by a skin graft. Another flap was outlined over the lower part of the buttock, based along the periphery of the anus.

X-ray examination of the pelvis showed a comminuted fracture of the left wing of the ilium with loss of substance in the upper portion of the defect. A fracture line extended from the defect down to just above the superior margin of the acetabulum. The anterior iliac fragment was rotated anteriorly and shifted downward. Another fracture line extended into the sacroiliac joint. Radiographic examination after a barium enema demonstrated the herniation of the descending colon (Fig. 2).

The patient wore a canvas corset and, by using crutches, was able to walk only a few steps. He complained of instability of his pelvic frame and the sensation that his "insides were falling out."

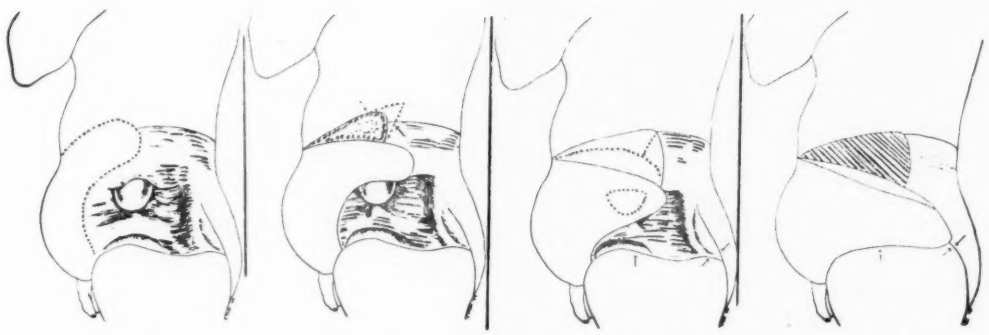

Fig. 3, *A*, *B*, *C*, and *D*.—Diagram depicting successive migration of flap.

The main feature of this case was a large intestinal hernia through a narrow, rigid aperture in the iliac wing. This was associated with complete loss of the overlying soft tissues, including skin.

The plan for resurfacing was complicated greatly by the loss of a considerable portion of the previously delayed flap. The remaining flap was obviously too small to be shifted directly into the desired position. The skin

over the buttock and the right of the spine was intact and could be advanced toward the soft tissue defect, but it could not be considered for the resurfacing of the region of the hernia. Therefore, it was decided to shift the flap in stages.

Because of the severe eczematoid dermatitis of the skin-grafted areas, several weeks elapsed before the patient was ready for surgery. On April 28, 1945, the flap was dissected. The inferior incision along the junction with the scarred area was extended down to the anterior iliac spine. The superior incision was prolonged to the anterior axillary line. The triangular flap was then advanced posteriorly and inferiorly without applying any tension. Posteriorly it was moved about 1½ inches toward the spine. Inferiorly it covered a strip of scarred area about 2 inches wide. This portion of the scar was excised, dissecting it superficially from the hernial sac. The flap was then sutured in its new position, joining it to the surrounding skin grafts. The secondary defect above was closed by approximating the superior and posterior borders. The skin graft along the posterior border did not interfere with closure since it was adherent to the thick pad of soft tissues from which it was not separated (Fig. 3, *A* and *B*).

The healing was uneventful. The patient was placed on an extended furlough. A reducing diet was recommended and the patient lost fifteen pounds.

With the flap alongside the hernial aperture and the vitality of the flap assured after repeated dissection, it was possible to combine the next stage of resurfacing with the repair of the hernia.

Fig. 4.—Photograph taken during the second stage showing the flap dissected. Hernial sac was freed and ready to be pushed inside pelvis. The epithelium around the hernia was not yet removed completely.

On Oct. 5, 1945, the upper flap was dissected again and fully mobilized. The scar and skin graft was stripped from the iliac and sacral bones and dissected superficially from the hernial sac. A V-shaped defect was exposed in the posterior iliac crest measuring 2 by 2½ by 3 inches. The fibrous cover was dissected from the hernial sac, freeing it completely (Fig. 4). The herniated bowel was readily pushed inside without opening the peritoneal cavity. The internal layer of periosteum was freed for some distance around the defect. The iliopsoas muscle lay along the posteromedial aspect. It was used to

obliterate the gap from the inside by pulling it laterally across the defect and securing it to the periosteum with interrupted sutures of 00 silk. The depression where the bone was missing was filled with a flap of muscle and subcutaneous tissue, most of it fibrotic. The flap was taken from the groin region and was based anterolaterally. The lower border of the external oblique muscle was then sutured over it, thereby buttressing the defect from the external surface (Fig. 5). The skin flap was basted down over the repaired region with interrupted sutures of cotton, No. 40.

The skin over the buttock and over the right side of the back was undermined and mobilized. These two skin edges were advanced along a V, suturing them to each other in the form of a Y until they reached the upper skin flap in its new position. The final closure was done with cotton No. 40 subcutaneously and silk on the skin surface. An effort was made to baste the skin flaps down to the underlying bare bone, using a few cotton sutures tacked down to some fibrous remnants on the bone. The secondary defect resulting from rotation of the flap was covered with a dermatome graft (Fig. 3, *C*). Pressure dressing was applied over the entire operative area, reinforced by a bivalved spica.

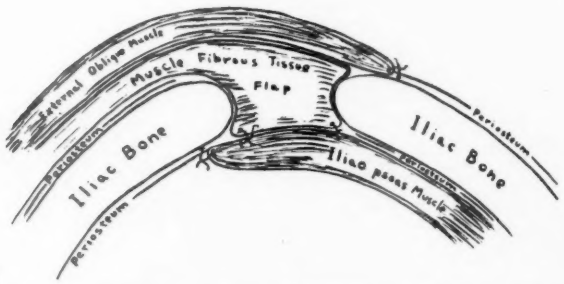

Fig. 5.—Diagram depicting obliteration of iliac defect.

Following this operation a sinus developed underneath the scar where the flaps failed to adhere to the underlying bone. Draining of this sinus and application of external pressure failed to obliterate it. It was therefore unroofed by incising the scar. The flaps were allowed to retract and the fibrous walls of the sinus were excised. On November 28, split grafts were applied to the exposed iliac and sacral bone. The take was poor and one month later an additional graft was done. It was not until the middle of February that the wound was epithelized completely and the patient sent out on furlough.

The partial failure of this operation was attributed to the fact that the skin flaps were sutured under slight tension and inadequate provision was made to keep them in close approximation with the underlying base. As a result, there was "tenting" of the flaps and creation of dead space underneath them, which in turn led to sinus formation. Since the floor of the sinus consisted of poorly vascularized sclerotic bone, and the scar between the flaps formed the roof, there was little tendency to form granulation tissue which would obliterate the sinus spontaneously.

It was felt that the second attempt to join the flaps should be performed in a clean field, after a few months interval to allow the flaps to recover. Therefore, a temporary resurfacing with thin split grafts was undertaken, although it was found very difficult and time consuming to make the temporary graft take on such a poor base.

The hernia was eliminated and the defect in the bone wall buttressed (Fig. 6). However, the lower iliac region and part of the sacrum were covered with a thin split graft adherent to the bone. These grafts were consid-

Fig. 6.

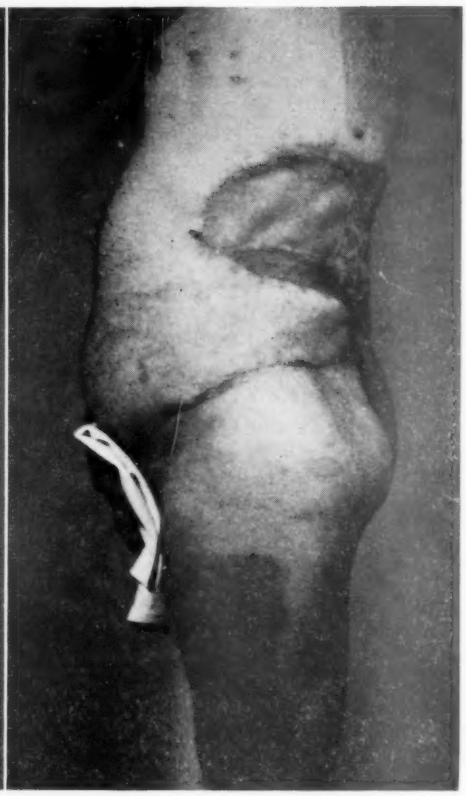

Fig. 7.

Fig. 6.—After second stage, hernia eliminated; flap covers entire region of hernia repair. (Courtesy of Army Institute of Pathology.)
Fig. 7.—Final condition.

Fig. 8.—X-ray view of pelvis two years after surgery; bony defect was obliterated by soft tissue. (Courtesy of Dr. Samuel Littman.)

ered unstable. The iliac and sacral regions, lacking soft tissue padding, were sensitive to pressure. This contributed in large measure to the patient's feeling of instability of his pelvic frame.

On April 4, 1946, the patient was operated upon again. The split grafts were stripped from the bone. The skin flap was dissected again and fully mobilized. It was advanced inferiorly and posteriorly until it lay without any tension alongside the gluteal prominence reaching the posterior skin border. The flap was not stretched by sutures above and below, but was allowed to contract, filling the irregularities of the bony contour. A dermatome graft covered the secondary defect above the flap (Fig. 3, *D*). The closure was done with subcutaneous cotton sutures and silk on the skin surface. The healing was uneventful. The patient was fitted with a re-enforced canvas belt and was referred for physical rehabilitation. His complaints were that the pelvis felt unsafe while he walked, and that he tired easily, both attributable to the iliac fractures. In August, 1946, he was discharged (Fig. 7).

The patient was examined again in June, 1948, two years after discharge. He had discarded the canvas belt, was able to walk without a limp for considerable distances, and could perform light physical work. Bowel function was normal. The defect in the bone could not be palpated, but was visualized readily by x-rays (Fig. 8).

SUMMARY

A case of a posterior intestinal hernia with extensive destruction of the surrounding soft tissue is described. The following features in the handling of this case deserve emphasis:

1. A large bony defect in the wing of the iliac bone was obliterated without recourse to foreign material, utilizing the surrounding soft tissue inside and outside the pelvis. The iliopsoas muscle was made to form the internal dynamic blockade, while the external oblique muscle was utilized for an outer dynamic layer. The intervening space was obliterated with static tissues which also re-enforced the closure. A firm stable repair was accomplished, and no recurrence could be noted when last examined two and one-half years after herniorrhaphy.

2. Extensive resurfacing of this area was coincidently effected with a well-padded contiguous flap. Since the only available contiguous flap was inadequate in size, it was rotated into the desired position in three stages. The repeated dissection of the flap (delaying) assured its vitality and made it possible, with each consecutive stage, to advance the flap further.

3. An attempt to suture the skin flap, even under the slightest tension, over an irregular base of sclerotic bone led to nonadherence of the flap and formation of a subcutaneous sinus. Excision of the tract, temporary skin grafting, and finally further advancement of the flap were necessary to complete an adequate resurfacing.

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THE HENRY APPROACH TO FEMORAL HERNIA

Report of Two Cases

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THE Henry approach is an unusual one; it is rarely described in surgical textbooks and infrequently used by surgeons, but it does offer many advantages in facilitating repair of a femoral hernia. Therefore, we wish to describe the extraperitoneal approach to femoral hernia as suggested by Henry and to report the cases of two patients seen at the Mayo Clinic in which this technique was satisfactorily employed.

The extraperitoneal approach to femoral hernia was first described by Henry[1] in 1936. He recognized the excellent possibilities of this approach for the first time when, in performing the operations for bilateral lesions of the lower portion of the urinary tract by means of the midline extraperitoneal approach, he noticed the remarkable anatomic exposure it presented of the femoral region. He himself said, "In a thin patient, as soon as my hand had displaced the peritoneum from beside the bladder, the view obtained of the four relevant structures, Gimbernat's ligament, the hinder edge of Poupart's, the fascia covering the pectineus and the external iliac vein was like that in a specimen prepared for a demonstration."

Fig. 1 demonstrates the view of the femoral hernia and its related anatomic structures obtained by means of Henry's extraperitoneal approach. First of all, optimal exposure is obtained by placing the patient in a modified Trendelenburg position. A low midline incision is made and after the recti muscles are separated, the unopened peritoneum is reflected from the lateral pelvic wall by blunt gauze dissection. The hernial sac, Gimbernat's ligament, Poupart's ligament, Cooper's ligament, the pectineal fascia, and the external iliac vein are easily identified. In most cases of incarcerated femoral hernia, Gimbernat's ligament must be incised in order to relieve the constriction about the neck of the sac. The exposure provided by means of the extraperitoneal approach makes it possible to do this easily without fear of injuring an anomalous obturator artery in the event one is present.

The femoral canal is easily repaired, with the ligamentous structures and neighboring vessels in clear view. Poupart's ligament is brought down and sutured to Cooper's ligament as far laterally as the external iliac vein. If there is too much tension on the sutures a small fascial flap can be raised from the pectineal fascia and coapted to Poupart's ligament. As a rule this procedure is not necessary.

REPORT OF CASES

Case 1.—A woman, 27 years of age, was admitted to the hospital on March 2, 1948. Her condition was acute. She complained of severe abdominal pain and vomiting of three

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hours' duration. Six years prior to admission, after a normal delivery, she had noted swellings in both groins. The swelling on the left side had disappeared; the one on the right persisted but could be reduced easily by the patient.

About three hours before admission, the patient experienced a sudden onset of generalized abdominal pain with vomiting. The mass in the right groin had become somewhat larger than usual, and it was hard, tender, and irreducible. She had passed gas and feces two hours before admission.

On examination the patient appeared to be in good general physical condition. Blood pressure was 134 mm. of mercury systolic and 80 mm. diastolic. The pulse rate was 90 beats per minute and the temperature was normal. The abdomen was soft, flat, and nontender. The peristaltic activity appeared normal. There was a firm, tender mass the size of an egg in the right femoral region. Reduction of the mass was not attempted. Further examination also revealed a small, easily reducible femoral hernia on the left side. Laboratory tests were within the normal range.

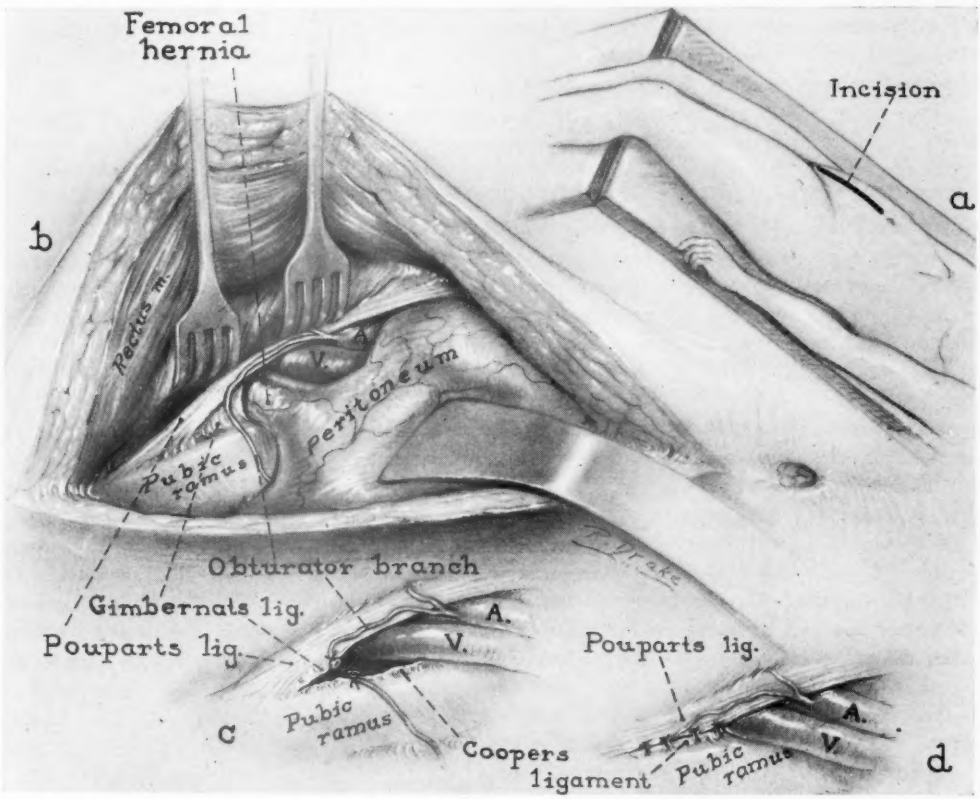

Fig. 1.—View of femoral hernia and its related anatomic structures obtained by means of the extraperitoneal approach of Henry.

A diagnosis of incarcerated femoral hernia on the right side and femoral hernia on the left was made and the patient was prepared for operation. In view of the presence of bilateral femoral hernia and the good condition of the patient, it was decided to use the extraperitoneal approach of Henry and to repair both hernias at the same time through one incision.

With the patient under spinal anesthesia and in a modified Trendelenburg position, a low midline incision was made. The recti were separated and the unopened peritoneum was reflected from the lateral pelvic wall on each side by blunt gauze dissection. The extraperitoneal exposure of the right and left hernial sacs and the entrance of each into its

respective femoral canal was excellent. On the right side, the neck of the sac which had been incarcerated was released by incising Gimbernat's ligament. The sac was opened and the content proved to be viable omentum which was readily replaced in the peritoneal cavity. The neck of the sac was ligated and the excess was excised. The sac of the femoral hernia on the left side was disposed of in a similar manner. The femoral canal on each side was then obliterated by coapting Poupart's ligament to Cooper's ligament as far laterally as the external iliac vein with nonabsorbable sutures.

The postoperative course was uneventful and the patient was dismissed from the hospital on the ninth postoperative day.

CASE 2.—A woman, 39 years of age, came to the clinic in July, 1948, because of a recurrent femoral hernia on the left side, of three months' duration. One year previous she had had an abdominal hysterectomy for fibroids and a repair of the femoral hernia elsewhere. Results of physical examination were essentially negative except for a swelling the size of a walnut in the left femoral region and thrombosed external hemorrhoids.

Because of a history of rectal bleeding and the presence of external hemorrhoids, proctologic examination was performed the next morning. External hemorrhoids and an acute angulation of the sigmoid were the only abnormalities noted in the rectum and colon. The procedure was moderately painful for the patient.

Two hours later the patient began to experience diffuse abdominal pain of moderate severity which was aggravated by deep respiration. Examination of the abdomen revealed marked tenderness and rebound tenderness across the entire lower portion of the abdomen, although the abdomen remained soft. The recurrent femoral hernia was easily reduced. The temperature was 99.8° F., the pulse rate was 80, and respirations were 20.

The patient was observed for a few hours, but in view of the fact that the abdominal pain and tenderness persisted, she was admitted to the hospital. A surgical consultation was held and because the possibility of perforation of the bowel could not be excluded, it was decided to perform an exploration.

Abdominal exploration revealed a considerable amount of thick, chocolate-colored fluid in the pelvic cul-de-sac. This was cleaned out and further exploration revealed a ruptured chocolate colored cyst of the left ovary, which had probably been the size of a tangerine. The lower portion of the sigmoid and the rectosigmoid were firmly adherent in the region of the cyst. In view of the patient's age, the previous hysterectomy, and the widespread endometriosis, all ovarian tissue was removed.

The recurrent left femoral hernia was repaired at the same time. The extraperitoneal approach of Henry was used and this was accomplished through the same incision. The parietal peritoneum was reflected from the left portion of the pelvic wall by blunt gauze dissection and the left femoral region was exposed. There was a small opening one-quarter inch in diameter lateral to Gimbernat's ligament in which there was a small hernial sac. The sac was reduced and obliterated and repair of the femoral canal was completed as described in the previous case. Exposure of the right femoral region revealed a moderately enlarged femoral canal. This was closed at the same time.

An uneventful postoperative course ensued.

SUMMARY

In the past there have been essentially two approaches to femoral hernia, namely, the inferior or femoral approach and the superior or inguinal approach, or some combination of these two. Henry's technique may be considered the third method of approach to femoral hernia. The following are some of the advantages offered by his extraperitoneal, midline exposure of the femoral canals:

1. It has been estimated that approximately 20 per cent of femoral hernias are bilateral.[2] In such cases the hernias can be repaired by this technique

through one incision. When a single femoral hernia is known to exist and this approach is used, it is possible to visualize the opposite femoral canal with ease and thus determine whether or not the defect is bilateral.

2. An abnormal obturator artery may be ligated under excellent exposure. This artery is present in 20 per cent[3] to 30 per cent[4] of the cases and is a real hazard, particularly in carrying out a femoral type of reduction and repair.

3. If ligation of the neck of the sac is carried out at its origin, a peritoneal dimple is not formed as a starting point of a recurrent hernia.

4. The contents of a strangulated femoral hernia are readily dealt with through this approach.

5. A femoral hernia may be repaired coincidentally with necessary surgical measures in the lower portion of the abdomen.

6. The Henry technique furnishes excellent exposure of anatomic structures adjacent to the femoral canal.

In an obese individual we would not advise that this technique of repair of femoral hernia be used routinely because the thick anterior abdominal wall makes exposure difficult. However, one of us (J. E. M.) recently combined the femoral and the midline approaches in repairing a large incarcerated femoral hernia on the right side of a man who weighed 240 pounds. Each approach complemented the other in this difficult operation.

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RESECTION OF SEGMENTS OF AURICULAR WALL

An Experimental Study

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CONSIDERABLE interest has now developed in the surgery of vascular anomalies involving the great vessels near the heart, patent foramen ovalis, acquired valvular disease of the heart, revascularization of the ventricular walls, etc. The surgery of cardiac tumors, however, has received scant attention and this is readily understood because of the rarity of these growths. Beck[1] cited an instance of successful resection of a localized tumorous mass on the left ventricular wall with relief of symptoms. Intracardiac neoplasms would, of course, present more technical difficulties. In a recent monograph entitled, *The Tumors and Polyps of the Heart,* Mahaim,[2] of Lausanne, apparently has reviewed all the literature on the subject including pathologic anatomy, physiology, and clinical diagnosis of all types of cardiac neoplasms. The ninth chapter of this work is essentially a theoretical discussion of the possibilities of surgical excision of cardiac neoplasms; the author strikes a somewhat optimistic note stating that if surgeons can remove emboli from the great vessels near the heart, it should not be a far step to excise an intracardiac papilloma, especially if the base is narrow and well circumscribed. On a recent occasion the problem of excision of an intra-auricular and presumably pedunculated papilloma producing a ball-valve action to temporary valvular obstruction was posed to one of us (A.B.) by Professor A. Vannoti, of Lausanne, such a diagnosis having been made clinically by him in a middle-aged male patient. The operation was never attempted; the patient since has died in a remote locality and necropsy was not obtained.

With no experience on our part in the technical problems of the surgery of the auricular wall in man, the experiments recorded below suggested themselves.

EXPERIMENTS ON RABBITS

Manipulation of the heart.

RB 1.—Weight 8 pounds, fourteen ounces. Chloroform anesthesia. No aseptic technique. Left chest opened by incision along lower left sternal margin. Pericardial sac incised to expose heart.

(a) Ventricles markedly compressed between fingers for 10 seconds. Slight dilatation of ventricles but resumption of normal beat.

(b) Repetition of (a). Increased dilatation of ventricles and return to normal beat.

(c) Entire heart compressed between fingers for 20 seconds. Marked dilatation of all chambers with failure to resume beat. Animal died.

RB 2.—Weight 7 pounds, 8 ounces. Ether anesthesia. No aseptic technique. Left chest opened as in RB 1.

Several rapid compressions of the entire heart were carried out and all chambers dilated markedly with death of the animal.

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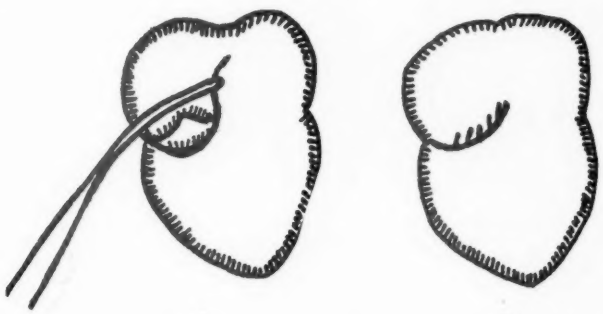
RB 3.—Weight 11 pounds. Ether anesthesia. No aseptic technique. Left chest opened as in RB 1 and RB 2. Heart exposed.

Auricles compressed with fingers for 15 seconds on two occasions. Return of normal beat but then rapid dilatation of all chambers. After second compression dilatation did not increase but heart became arrested and rabbit died. Opening and closure of isolated portion of left auricle.

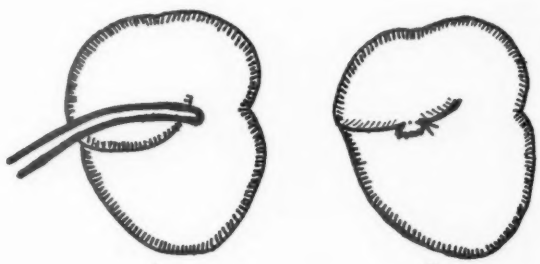
RB 4.—Weight 10 pounds, 8 ounces. Ether anesthesia. No aseptic technique. Left chest entered as in previous experiments. Heart exposed. A rubber-shod small curved hemostat was placed transversely across base of left auricular appendage. The isolated portion of the latter was opened, interior examined, and the opening then closed with a continuous stitch of 00 silk on a curved atraumatic needle. The clamp was removed and isolated portion of auricle again filled with blood. Heartbeat apparently normal. Seven weeks later the animal was alive and active (Fig. 1).

Ligature isolation of auricular appendage with excision of isolated segment (Figs. 2 and 3).



A. *B.*

Fig. 1.—Diagrammatic illustration of experiment RB 4. *A*, Rubber-shod small curved hemostat applied to base of auricular appendage. The latter has been split and interior examined. *B*, Incision has been repaired by continuous suture and clamp removed. Normal heartbeat. Animal survived.



A. *B.*

Fig. 2.—Diagrammatic illustrations of experiments. RB 1 and those following. *A*, Clamp placed across base of auricular appendage. *B*, Ligature applied beneath clamp and latter removed. Portion of auricular appendage distal to clamp cut away.

RB 1A and *RB 2A.*—In these animals the left side of the chest was opened under ether anesthesia. No aseptic technique. A silk ligature was placed about the base of the left auricular appendages beneath a curved hemostat which was applied transversely across their bases. The ligature was tied, thus closing the appendage and the portion of the auricular wall distal to the ligature was cut away (Fig. 3). These measured 5 to 10 mm. in length. The hearts apparently continued to beat normally. The animals died in twenty-six and forty-eight hours, respectively. Necropsy revealed widespread mediastinitis. (Aseptic technique had not been employed during operations.)

RB 1B, RB 2B, and *RB 3B.*—Experiments as before. One animal died during the experiment (anesthesia) and in the second the auricle was traumatically ruptured, with death from hemorrhage. The third animal survived and was normal during an observation period of several weeks.

RB 1C, RB 2C, RB 3C, RB 4C, and *GR.*—Experiments as before. No aseptic technique. Two animals survived and were well ten days after operation. Two died during the operation of bilateral pneumothorax and accidental severance of a pulmonary artery, respectively. One survived six weeks and died of left empyema.

EXPERIMENTS ON DOGS

Dogs of both sexes were anesthetized with nembutal and ether (positive pressure). With regular aseptic procedure a linear incision was made along the left margin of the sternum to enter the chest cavity and expose the pericardial sac. The anterior surface of the latter was grasped with two hemostats and between them a small incision made which was enlarged to exposure of the anterior aspect of the heart.

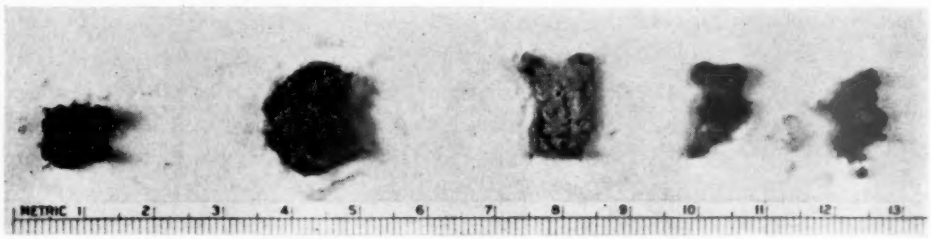


Fig. 3.—Photograph of formalin-hardened segments of auricles and auricular appendages excised in experiments on rabbits. (See text.)

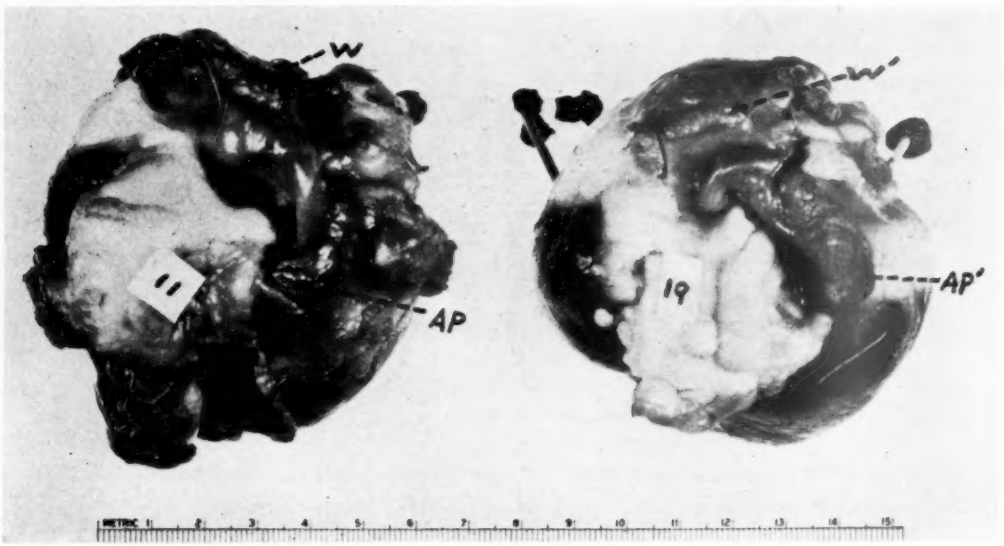


Fig. 4.—Photograph of hearts from Dogs 11 and 19. Animals were sacrificed six weeks after one auricular appendage was excised as shown in Fig. 2. *AP* and *AP'*, intact auricular appendages; *W* and *W'*, sites of healed wounds resulting from excision of auricular appendages.

The margin of the tip of the right auricle was grasped with a large curved hemostat and the whole auricle pulled upward. Another curved hemostat was applied to the base of the auricle transversely and that portion of the auricle above the clamp cut away. A ligature was applied beneath the clamp and tied. The pericardial sac was then closed (Fig. 4).

Following the operation the heart exhibited no appreciable change nor showed even a slight general dilatation.

More details of the protocols are summarized as follows:

Dog 11.—Convalescence uneventful. Disposed of six weeks after operation with no apparent abnormality.

Dog 12.—Recovery from operation satisfactory. On sixth day chest wound appeared infected and bled. On the ninth postoperative day the animal appeared very ill and was sacrificed. Necropsy revealed bilateral lobar pneumonia and infected wound in chest wall. Wound in heart healed and clean.

Dog 13.—Convalescence uneventful. Disposed of dog nine weeks after operation. No abnormality at this time.

Dog 14.—Upon incision of pericardial sac there seemed to be dense adhesions obliterating the pericardial cavity. When these were being separated, a large rent was produced in the auricle with excessive hemorrhage, rapid collapse of the animal, and death.

Dog 19.—Convalescence uneventful. Dog disposed of six weeks after operation. No abnormality.

Dog 21.—Convalescence uneventful. Dog disposed of six weeks after operation. No abnormality.

DISCUSSION

Portions of the ventricular wall were successfully excised in the dog by Murray[3] after preliminary vascular occlusion. As mentioned previously, Beck successfully removed a tumorous mass from the ventricular wall of a human patient.

In the rabbit experiments just summarized, it was shown that marked compression of the heart for periods of 15 to 20 seconds was followed by dilatation of all chambers and, when the compression was repeated, by death. One experiment demonstrated that a portion of the auricle could be temporarily isolated by compression, and opened and closed by suture without apparent permanent disturbances. A third series of experiments illustrated the feasibility of excision of part of the auricular appendage distal to a clamp with repair of the clamped segment. Similar experiments on a series of dogs carried out with aseptic technique also showed the feasibility of removal of a large segment of auricular appendage without interruption of normal heart action and with prolonged survival of the animals.

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DELAYED PRIMARY CLOSURE OF CONTAMINATED WOUNDS

A Report Based on Forty-six Cases

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IN SPITE of recent advances made in the management of wounds of all types there remains a high incidence of postoperative infections in grossly contaminated wounds. Primary closure of surgical incisions is usually followed by uninterrupted healing, but wounds contaminated by frank pus, or by the contents of the lower gastrointestinal tract, especially the colon, often become infected if closed primarily.

Secondary closure is the term applied to the technique of the delayed closing of a wound by revision and suture, that is, by mobilizing the retracted skin margins and excising the granulation tissue in the base of the wound. Delayed primary closure may be defined as the technique of closing surgical incisions, or accidental wounds previously prepared, after a period of delay but without revision being necessary. A delayed primary closure may be done from twenty-four hours following the original preparation of the wound until five or six days later.[1] After six days the skin margin will begin to retract inward and granulation tissue will appear in the wound, making secondary closure necessary.

Primary closure of previously débrided wounds after a period of delay was first used by French surgeons during World War I.[3] Their technique consisted of primary débridement, flavine pack, and closure in six days. A culture was taken twenty-four hours after the primary débridement and if hemolytic streptococci were found the wound was left open. The advantages of this procedure were (1) the practical elimination of gas bacillus infection and (2) marked diminution in the number of pyogenic infections. The disadvantages were the possibility of secondary contamination of an open wound and the necessity of two operations instead of one. The advantages far outweighed the risk of infection incurred in primary suture of doubtful wounds.[2]

This technique of delayed primary closure was revived by Coller for the management of grossly contaminated operative incisions, especially those contaminated by the contents of the lower gastrointestinal tract. Where primary closure was done he reported an incidence of 50 per cent infection in wounds contaminated by the contents of the lower bowel. This was true in spite of the fact that it was customary to use a drain. In Coller's series delayed primary closure was done in twenty-one cases. There was uninterrupted healing in all patients except one who developed a trivial infection.[3]

The same organisms may be grown at the time of completion of a delayed closure that were present originally in these grossly contaminated wounds. This suggests that the technique does not have a bactericidal or bacteriostatic effect, but in some way prepares the wound so that it is more resistant to invasion by

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the organisms present.[1] Even when infection occurs it tends to remain localized to the surface of the wound without the production of a spreading cellulitis.[3] It has been shown by duMortier that incisions in the abdominal wall of guinea pigs contaminated with *Staphylococcus aureus hemolyticus* have little resistance to bacterial invasion during the first six hours. After the wounds had been closed twelve hours and the bacteria applied, there was infection but it usually remained localized. From this time onward, the percentage of severe infection steadily decreased for the next five days, after which time it was no longer possible to infect these wounds by swabbing organisms on the surface.[10, 11]

There is a minimum of devitalized tissue in surgical incisions, but in spite of adequate hemostasis and wound coaptation there remains a variable amount of blood clot and serum in the wound, especially in the fatty subcutaneous tissue. This blood clot and serum provide a medium for growth of all types of aerobic bacteria. Devitalized tissue, although small in amount, provides favorable circumstances for the growth of anaerobic organisms.[6] It has long been known that granulation tissue is more resistant to all types of organisms than are unprotected raw wound surfaces. Thus, by primary delayed closure one removes the majority of wound pabulum and provides the wound surfaces with a protective coating of fibrin, leucocytes, and beginning capillary buds.

The wounds selected for delayed primary closure in this series were grossly contaminated either with pus or with contents of the gastrointestinal tract. If closed primarily one would expect a high incidence of serious wound infection with such contamination.

The technique used by us is similar to that described by Coller (Fig. 1). The peritoneum and fascia are closed with interrupted cotton sutures. Vertical mattress sutures of single filament nylon are then placed deeply through the fat and skin so that alternate sutures can be tied on opposite sides of the wound. This prevents tangling of the ends of the sutures which are left long to be tightened later. Two small packs are introduced from opposite ends of the incision, beneath the sutures, meeting in the center of the wound. The sutures are tied loosely with a double twist, single knot, care being taken not to approximate the skin edges. Arbitrarily forty-eight hours is selected as the period of delay before removing the pack and completing the closure.[8] This is done at the patient's bedside using only mild sedation.[4, 5]

At first, fine mesh gauze was used for the pack, but this later was replaced with rayon gauze 114 by 114 mesh as described by Owens.[12] This material was chosen because it can be removed with less trauma to the wound margins. Its coefficient of friction is low and the mesh is fine enough to prevent ingrowth of capillary buds but coarse enough to allow for the absorption of serum and blood.[12] The rayon gauze pack was saturated with penicillin, penicillin and streptomycin, or normal saline solution.[7, 9] A drain was left in the abdominal cavity in some cases and beneath the anterior rectus sheath in others. In all the cases in which drains were used the drains were brought out through the wound.

From Table I it may be seen that in this series of forty-six consecutive contaminated wounds there were fourteen infections. Six of these were trivial,

TABLE I

NO.	NAME	DIAGNOSIS	OPERATION	HEALING	DAYS DELAYED
1	F. J.	Ventral hernia, cellulitis of skin	Fascial overlap	Trivial infection	None
2	L. H.	Intestinal obstruction perforation of ileum	Drainage of abscess, freeing of adhesions	No infection	None
3	J. J.	Umbilical hernia, erosion of skin over hernial sac	Mayo hernioplasty, repair of intestine	No infection	None
4	P. Y.	Strangulated hernia, gangrene of ileum	Resection of ileum	No infection	None
5	R. S.	Postoperative strangulated hernia	Fascial overlap	No infection	None
6	H. B.	Obstructing duodenal ulcer	Partial gastrectomy	No infection	None
7	G. W.	Perforated duodenal ulcer generalized peritonitis	Gastrorrhaphy	No infection	None
8	A. H.	Obstructing duodenal ulcer	Partial gastrectomy	No infection	None
9	T. M.	Carcinoma of sigmoid colon	Obstructive resection	No infection	None
10	T. W.	Carcinoma of sigmoid colon	Closure of colostomy	Trivial infection	None
11	L. C.	Carcinoma of rectum with obstruction	Second stage Lahey resection	No infection	None
12	J. N.	Carcinoma of sigmoid colon	Closure of colostomy	No infection	None
13	T. C.	Acute appendicitis with perforation	Appendectomy, drain beneath fascia	No infection	None
14	G. R.	Perforated appendix with appendical abscess	Appendectomy and drainage of abscess	Serious infection	20
15	O. S.	Acute appendicitis with perforation	Appendectomy	Serious infection	7
16	L. T.	Obstructing duodenal ulcer	Partial gastrectomy	No infection	None
17	L. P.	Acute appendicitis with perforation	Appendectomy	No infection	None
18	H. B.	Acute appendicitis with perforation	Appendectomy	No infection	None
19	A. R.	Acute appendicitis with perforation	Appendectomy, peritoneal drain	Trivial infection	4
20	R. S.	Perforated appendix, generalized peritonitis, appendical abscess	Appendectomy and drainage of abscess	Serious infection	22
21	R. K.	Obstructing duodenal ulcer	Partial gastrectomy	No infection	None
22	J. T.	Obstructing duodenal ulcer	Partial gastrectomy	No infection	None
23	M. S.	Obstructing duodenal ulcer	Partial gastrectomy	No infection	None
24	W. B.	Carcinoma of sigmoid colon	Primary resection	No infection	None
25	W. B.	Carcinoma of sigmoid colon	Closure of colostomy	No infection	None
26	R. R.	Diverticulitis of sigmoid colon with perforation	Obstructive resection	Trivial infection	7
27	P. S.	Obstructing duodenal ulcer	Partial gastrectomy	Trivial infection	None
28	J. M.	Stab wound of abdomen with perforation of ileum	Repair of perforation, drain beneath fascia	Serious infection	7

TABLE I—CONT'D

NO.	NAME	DIAGNOSIS	OPERATION	HEALING	DAYS DELAYED
29	E. M.	Sarcoma of sigmoid and ileum	Obstructive resection	No infection	None
30	E. M.	Sarcoma of sigmoid and ileum	Closure of colostomy	Trivial infection	4
31	J. W.	Intussusception, gangrene of ileum and cecum	Closure of colostomy	No infection	None
32	R. T.	Gunshot wound of the abdomen, perforation of rectum and ileum	Repair of perforation, colostomy	No infection	None
33	R. T.	Gunshot wound of the abdomen, perforation or rectum and ileum	Closure of colostomy	No infection	None
34	H. B.	Perforated appendix, generalized peritonitis	Appendectomy, peritoneal drain	Serious infection	14
35	B. R.	Perforated appendix	Appendectomy	No infection	None
36	L. D.	Strangulated ventral hernia	Mayo hernioplasty	No infection	None
37	W. T.	Obstructing duodenal ulcer	Partial gastrectomy	No infection	None
38	A. W.	Carcinoma, head of pancreas	Cholecystojejunostomy	No infection	None
39	G. S.	Carcinoma of sigmoid colon	Closure of colostomy	No infection	None
40	E. M.	Obstructing duodenal ulcer	Partial gastrectomy	No infection	None
41	H. H.	Ovarian cyst, perforation of sigmoid	Repair of perforation, peritoneal drain	Serious infection	11
42	H. H.	Fecal fistula	Resection of fistula, repair of sigmoid	No infection	None
43	W. N.	Perforated appendix	Appendectomy	No infection	None
44	H. B.	Carcinoma of stomach	Partial gastrectomy	No infection	None
45	A. A.	Perforated duodenal ulcer	Gastrorrhaphy, drain beneath fascia	Serious infection	14
46	W. P.	Gunshot wound of abdomen, perforation of sigmoid and ileum	Repair of perforation, drain beneath the fascia	Serious infection	8

there being a serous discharge but no delay in wound healing. There were eight serious infections with a delay of from seven to twenty-two days in wound healing. However, in four of these, intra-abdominal drains were brought out through the wound and the continued drainage of purulent material from the peritoneal cavity contributed to the wound infection. In three of these serious infections drains were left beneath the fascia and brought out through the wound. In nearly every case in which a drain was brought out through the wound an infection occurred. In only one case was there a serious infection in which a drain was not used.

Drains should be used infrequently, but when it is deemed necessary to leave a drain within a localized intraperitoneal abscess, it should be brought out through a separate stab wound to prevent continued contamination of the incision. If a drain must be left beneath the anterior rectus sheath, it too may be brought out through a separate stab wound. However, it would seem that the occasion for leaving a drain beneath the anterior rectus sheath should be infrequent, since the resistance of this tissue to infection is high as compared to the fat and subcutaneous tissue.

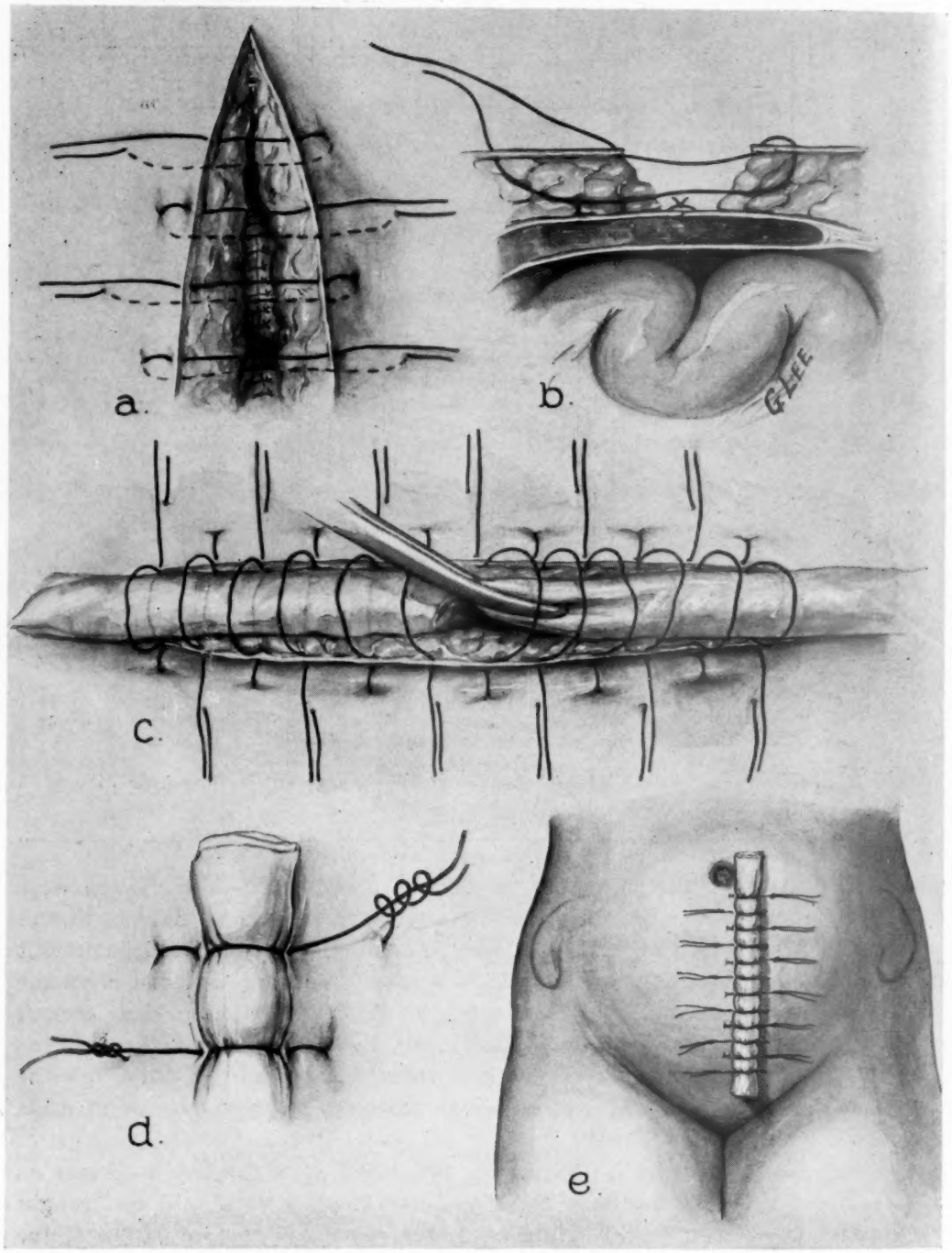

Fig. 1.—Technique of delayed primary closure. *a* and *b*, Peritoneum and fascia closed; interrupted vertical mattress sutures placed through skin and subcutaneous fat. *c*, Rayon gauze pack introduced beneath sutures from each end of wound. *d*, Sutures tied loosely with single triple throw knot. *e*, Final appearance of wound. (Any rubber drains used are brought out through a separate stab wound.)

The incidence of infection both serious and trivial in this series of cases is 30.4 per cent. Eight, or 17.4 per cent, were serious infections with the majority occurring in wounds in which drains were used.

It is not possible from this study to determine the value of penicillin and streptomycin locally, but it would seem that these two antibiotics in aqueous solution might be of value in conjunction with delayed primary closure.

CONCLUSIONS

1. Delayed primary closure will lower the incidence of infection in grossly contaminated surgical incisions.

2. Of the infections that occur, a high percentage will be trivial without delay in wound healing.

3. Drains from within the abdomen or beneath the anterior rectus sheath should be brought out through a separate stab wound.

4. Rayon gauze is an ideal pack because there is minimal amount of trauma on removal.

5. It would seem that penicillin and streptomycin in aqueous solution have some antibacterial effect and help to prevent subcutaneous infections if used locally in conjunction with a rayon pack.

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STREPTOMYCIN THERAPY IN ESTABLISHED WOUND INFECTIONS

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INTRODUCTION

THIS is an analysis of 200 cases of streptomycin-treated nontuberculous infections of soft tissues in hospitals of the United States Army. It corroborates and suplements an earlier report.*

RESULTS

The bacterial flora cultured from 172 of the 200 cases are listed in Table I. There were 28 acute infected closed wounds not cultured; these were presumably coccal in origin. *Staphylococcus aureus* was predominant. Two-thirds of the lesions had a mixed flora.

Out of 200 cases, 135 patients were given streptomycin alone. The remaining 65 were being treated also with penicillin, even though penicillin alone had been ineffective.

The results show that 52 per cent of all patients benefited. The response was doubtful in another 11 per cent and negligible in the remaining 37 per cent. Response to therapy was indicated by the pathogenesis of the lesion. The pathogenesis fell into three groups: (1) cellulitis, (2) superficial and deep abscesses, and (3) miscellaneous. Description of the response by the various groups follows:

Group I, Cellulitis (Table II).—Lesions with cellulitis occur over a large area and may suppurate. Of the 52 patients treated, 90 per cent benefited with either streptomycin alone or with streptomycin plus penicillin. The 10 per cent listed as doubtful or failures were acute flares in scar tissue. Adjuvant measures were limited to needle aspiration or stab-wound drainage. The results thus compared favorably with those obtained with penicillin alone. The usual dose of streptomycin was 2 Gm. daily, given in four doses, for from four to seven days. Untoward reactions were rare with this dosage.

Group II, Superficial and Deep Abscesses (Tables III and IV).—Lesions of superficial and deep abscesses are grouped together because their response to therapy is similar.

The abscesses in the 51 cases (Table III) occurred in traumatic wounds, the urinary system, and as furuncles and carbuncles. Best results took place in infected traumatic wounds, where 61 per cent were benefited. Improvement in the urinary tract lesions was only 33 per cent, and with furuncles and carbuncles only 20 per cent.

For adequate response the following measures were necessary: (1) free drainage, and (2) appropriate excision of dead tissue. Failure with strepto-

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TABLE I. BACTERIOLOGY OF 172 CASES OF WOUND SUPPURATION*

ORGANISM	TOTAL	PURE		MIXED	
		NUMBER	PER CENT	NUMBER	PER CENT
Staphylococcus aureus	131	34	26	97	74
Streptococcus beta hemolytic	21	2	10	19	90
Streptococcus nonhemolytic	34	3	9	31	95
Escherichia coli	39	12	31	27	69
Klebsiella pneumonia (Friedländer's)	30	8	27	22	73
Proteus vulgaris	41	3	7	38	93
Pseudomonas pyocyanea	17	2	12	15	88
Others	3	2	66	1	34

*Twenty-eight closed lesions not cultured.

TABLE II. GROUP I, RESULTS OF THERAPY IN 53 WOUNDS WITH CELLULITIS

DIAGNOSIS	STREPTOMYCIN ALONE				STREPTOMYCIN WITH PENICILLIN			
	NUMBER OF CASES	BENEFITED	DOUBTFUL	NOT BENEFITED	NUMBER OF CASES	BENEFITED	DOUBTFUL	NOT BENEFITED
Cellulitis	18	17	0	1	8	8	0	0
Cellulitis with suppuration	21	17	1	3	6	6	0	0
Total	39	34	1	4	14	14	0	0

TABLE III. GROUP II, RESULTS OF THERAPY IN 51 SURGICAL ABSCESSES

	NUMBER OF CASES	BENEFITED		DOUBTFUL		NOT BENEFITED	
		NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Traumatic wounds	23	14	61	3	13	6	26
Carbuncles and furuncules	16	3	19	4	25	9	56
Urinary system	12	5	42	1	8	6	50
Total	51	22	43	8	16	21	41

TABLE IV. GROUP II, RESULTS IN 81 POSTOPERATIVE WOUND INFECTIONS

DIAGNOSIS	NUMBER OF CASES	BENEFITED		DOUBTFUL		NOT BENEFITED	
		NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Abdominal wall	22	10	45	2	10	10	45
Flank	12	5	42	1	8	6	50
Perineum	6	1	16	1	16	4	67
Wound revisions	41	18	43	6	14	17	42
Total	81	34	42	10	12	37	46

mycin was associated with: (1) recurrence of infection in scar, (2) dead tissue, (3) constant source of reinfection from fistula or sinus, and (4) inadequate drainage.

The 81 postoperative wound infections (Table IV) accounted for 40 per cent of our cases. Of these lesions, 80 per cent developed under the prophylactic use of penicillin. In 46 cases treatment was by streptomycin alone and in the other 35 a combination of streptomycin and penicillin was used; 42 per cent of the patients were benefited, 13 per cent were doubtfully benefited, and 45 per cent were unaffected. The results with either penicillin plus streptomycin or streptomycin alone were similar.

The postoperative infections included 22 of the abdominal wall, 12 of the flank, 6 of the perineum, and 41 wound revisions. One-half of the nonhealing

abdominal wounds were complicated by fecal fistulas. The usual daily dose of streptomycin was 2.5 Gm. for from seven to ten days.

Poor results accompanied the following: (1) fecal fistulas; (2) foreign bodies, as bone chips, plastics, silk, and cotton or metal; (3) urinary fistulas, and (4) sloughing perineal wounds.

Group III, Miscellaneous Wound Infections (Table V).—The miscellaneous infections gave the least response to streptomycin. Thus, unsatisfactory results occurred in cutaneous gangrene, Buerger's disease, chronic tenosynovitis, chronic burns, chronic ulcers, and chronic fistulas. In the 4 patients doubtfully benefited, 2 with ecthyma and 2 with decubitus ulcer, streptomycin apparently initiated improvement, but bacteria persisted and wound healing did not occur. The wounds were closed by excision and grafting.

TABLE V. GROUP III, RESULTS OF THERAPY IN 15 MISCELLANEOUS WOUND INFECTIONS TREATED WITH STREPTOMYCIN

DIAGNOSIS	NUMBER OF CASES	BENEFITED	DOUBTFUL	NOT BENEFITED
Ecthyma	2	0	2	0
Decubitus ulcer*	2	0	2	0
Chronic burns (second and third degree)	3	0	0	3
Buerger's disease	3	0	0	3
Sinus and fistula	4	0	0	4
Acute tenosynovitis	1	0	0	1
Total	15	0	4	11

*One patient treated with streptomycin and penicillin.

Topical application of streptomycin as ointments, packs, and irrigations has been ineffective in our hands. Bacteria, especially cocci, pyocyaneus, and proteus, in infected sloughing and granulation tissue may become streptomycin-fast within one or two days. If bacteria are not eliminated from wounds after two or three applications of streptomycin, further local treatment is useless.

SUMMARY

1. Over-all benefit in 200 streptomycin-treated nontuberculous infections of soft tissues was 52 per cent.

2. Patients who were treated also with penicillin showed no greater benefit.

3. Of the patients with cellulitis, 90 per cent benefited from streptomycin therapy.

4. Superficial and deep abscesses required adjuvant measures for beneficial response. Of the patients with infected traumatic wounds, 61 per cent were benefited. Furuncles and carbuncles improved in only 20 per cent of the cases, while infections connected with the urinary tract were suppressed in only 33 per cent of the cases.

5. In postoperative wound infections, 42 per cent were benefited. Factors which contributed to poor results are listed.

6. Miscellaneous infections (cutaneous gangrene, Buerger's disease, chronic tenosynovitis, chronic burns, chronic ulcers, and chronic fistulas) had least response to streptomycin.

7. Topical application of streptomycin was of no value.

8. The recommended dosage is 2.0 to 2.5 Gm. streptomycin q.i.d. for four to eight days. Toxic reactions are uncommon with this dosage.

CONCLUSIONS

Streptomycin is of benefit in surgical infections, yet it is not a panacea. It is most effective in cellulitis, but only moderately effective in cases of adequately drained superficial and deep abscess. The most beneficial effects of therapy are observed in acute infections when the drug is given early in the disease. Thus, the principal uses of the drug are for gram-positive and mixed infections in which there has been no response to maximal doses of penicillin within forty-eight to seventy-two hours, or earlier, if in vitro evidence of penicillin resistance can be secured. In chronic suppurating lesions the drug is useful only as an adjuvant to drainage and section of compromised tissue for the suppression of residual bacteria. In our experience, topical application of streptomycin has not given good results.

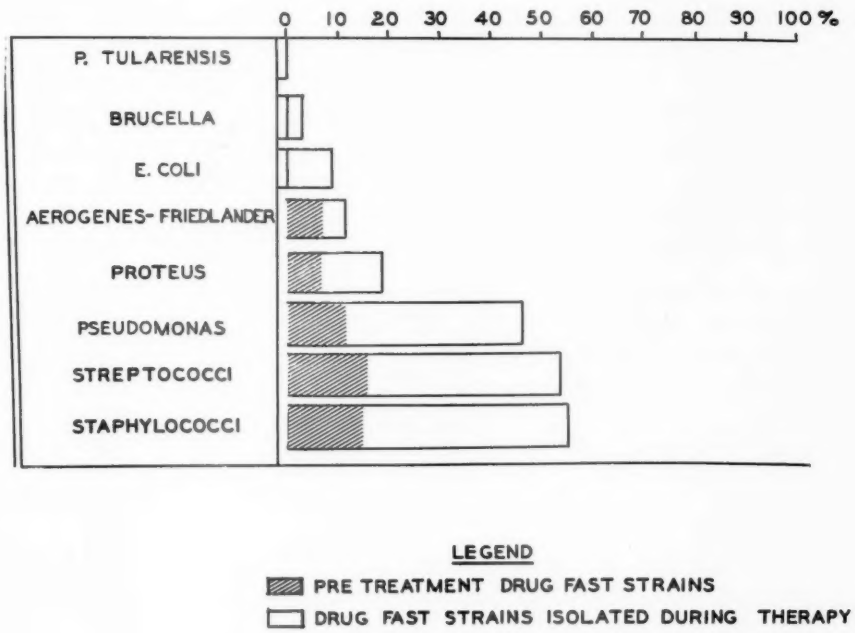

Fig. 1.—Streptomycin-fastness in vivo.

Two-thirds of open pyogenic surgical infections are polybacterial. Careful bacteriologic analysis of the wound bacteria and culture sensitivity testing are necessary prerequisites to successful streptomycin therapy. This antibiotic has inhibitory action on most aerobic gram-negative and gram-positive surgical organisms, but wide variation in susceptibility is observed, and initially streptomycin-fast organisms are found (Fig. 1). Drug-fastness is a common factor in unsatisfactory therapeutic responses. For this reason, the drug should be used only when properly indicated. The requisites for successful streptomycin therapy are: (1) streptomycin-sensitive organisms, (2) a dosage of at least 2.0 Gm. a day, (3) adequate blood supply, and (4) absence of necrotic tissue.

THE NEPHROTOXICITY OF BACITRACIN* IN MAN

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THE nephrotoxicity of parenterally administered bacitracin in animals has been well established.[1, 3] The degree of nephrotoxicity of systemically administered bacitracin in man, however, has not been definitely confirmed. Scudi, Coret, and Antopol[3] concluded that bacitracin produced serious renal damage in mice but that it was considerably less nephrotoxic in monkeys. In monkeys necrotic renal tubule cells were found in two of the five animals studied. In 105 patients who had received bacitracin systemically for the treatment of surgical infections the evidences of nephrotoxicity were not conclusive.[4] Phenosulfonphthalein excretion tests, determinations of urea nitrogen or nonprotein nitrogen concentration in the blood, and frequent urinalyses in a number of these patients did not demonstrate definite impairment of renal function.[4, 5] Renal damage was suspected, however, because of the frequent occurrence of albuminuria, the less frequent appearance of cellular elements and casts in the urine, and the occasional development of oliguria or anuria. It was not possible to state categorically whether the oliguria or the anuria observed was the result of bacitracin therapy, the infectious process, or whether they were the sequelae of anesthesia and operation.

It was thought advisable to determine the functional capacity of the kidney before and after parenteral bacitracin therapy in patients who did not have infections. Glomerular filtration rate, maximal tubular reabsorption of phosphate, maximal tubular excretion of para-aminohippurate, and renal plasma flow were determined before and after systemic bacitracin therapy in ten volunteer, convalescent surgical patients with no signs or symptoms of infection or renal disease, and no prior evidence of functional renal impairment.

PROCEDURE

Sodium thiosulfate[6] was used to measure the glomerular filtration rate. Maximal tubular reabsorption of phosphate was determined after doubling the initial blood phosphate concentration.[7, 8] Maximal tubular excretion and effective renal plasma flow were determined, the former at high and the latter at low blood para-aminohippurate concentrations.[9] All blood samples for these determinations were taken from an indwelling arterial needle. Marked changes in blood concentrations were prevented by a constant intravenous infusion of the agents used.

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*The bacitracin was kindly supplied to us by Commercial Solvents Corporation, New York, N. Y.

In the five patients of the acute experimental group glomerular filtration rate and maximal tubular reabsorption of phosphate were measured for three consecutive ten-minute periods before bacitracin was administered. Then 2,000 units of bacitracin were administered intravenously in one to two minutes followed by the administration of 360 units of bacitracin per minute for approximately one hour. During the latter period the same renal function studies were repeated for six consecutive ten-minute periods. As effective renal plasma flow and maximal excretion of para-aminohippurate cannot be measured simultaneously, the former renal function was determined in Patients 1, 2, and 3 and the latter in Patients 4 and 5.

In the "chronic" experiments all of the renal functions described were determined in each of the six patients before and after the intramuscular administration of bacitracin. Patients 1, 2, 3, 4, and 5 received 49,000 to 50,000 units of bacitracin every six hours for four to thirteen days. Patient 6 received three doses of 50,000 units of bacitracin intramuscularly for two consecutive days, none for the next six days, and then four injections of 50,000 units each in the twenty-four hours preceding the final renal function tests. In two patients, 1 and 3, the studies were repeated two and four weeks, respectively, after the administration of bacitracin had been discontinued. After bacitracin therapy in Patient 5 the total renal plasma flow was also measured according to the Fick principle[10] by determining the arteriovenous difference of para-aminohippurate concentration in the peripheral arterial and the renal

TABLE I. RENAL FUNCTION STUDIES BEFORE AND AFTER BACITRACIN THERAPY—ACUTE EXPERIMENTS

NO. OF PATIENT	SEX	AGE (YR.)	PERIOD OF OBSERVATION	GLOMERULAR FILTRATION RATE (C.C. PER MIN.)	RENAL PLASMA FLOW (C.C. PER MIN.)	TUBULAR EXCRETION (MG. PER MIN.)	TUBULAR REABSORPTION (MM. PER MIN.)	FILTRATION FRACTION (PER CENT)
1	M	40	Before bacitracin	133	774	---	0.185	17.2
			First half hour	134	816	---	0.183	16.4
			Second half hour	133	537	---	0.179	24.8
2	M	41	Before bacitracin	120	562	---	0.099	21.4
			First half hour	136	703	---	0.101	19.3
			Second half hour	124	600	---	0.088	20.7
3	M	50	Before bacitracin	129	580	---	0.104	22.2
			First half hour	156	586	---	0.139	26.6
			Second half hour	126	535	---	0.100	23.5
4	F	22	Before bacitracin	159	---	84.5	0.160	---
			First half hour	158	---	83.8	0.166	---
			Second half hour	150	---	78.4	0.157	---
5	F	37	Before bacitracin	123	---	80.7	0.091	---
			First half hour	122	---	71.5	0.090	---
			Second half hour	134	---	69.0	0.105	---

Each value recorded is the average of three consecutive ten-minute blood and urine collection periods. After determination of the renal functions before therapy each patient received 2,000 units of bacitracin intravenously in a period of one to two minutes immediately followed by 360 units of bacitracin per minute by constant intravenous drip method for a period of one hour.

All values have been corrected to a skin surface of 1.73 square meters. No corrections have been made for body temperatures because the temperatures of these patients were all between 98° and 99° F.

TABLE II. RENAL FUNCTION STUDIES BEFORE AND AFTER BACITRACIN THERAPY—CHRONIC EXPERIMENTS

NO. OF PATIENT	AGE (YR.)	SEX	PERIOD OF OBSERVATION BEFORE AND AFTER BACITRACIN	GLOMERULAR FILTRATION RATE (C.C. PER MIN.)	RENAL PLASMA FLOW (C.C. PER MIN.)	TUBULAR EXCRETION (MG. PER MIN.)	TUBULAR REABSORPTION (MM. PER MIN.)	TOTAL BACITRACIN ADMINISTERED IN UNITS	DAYS DURATION OF BACITRACIN ADMINISTRATION (IN DAYS)	MFGRS. LOT OF BACITRACIN
1	47	M	Before	89.5	336	54.4	0.221	2,558,000	13	B
			After	53.7	235	22.8	0.054			
			28 Days later	71.4	356	42.7	0.078			
2	28	F	Before	125.0	1020	77.8	0.100	1,960,000	10	B
			After	78.0	371	28.6	0.027			
3	67	F	Before	79.0	775	56.2	0.058	1,600,000	8	A
			After	43.7	103	8.3	0.019			
			12 Days later	48.5	224	19.1	0.29			
4	16	M	Before	229.0	1052	60.1	0.227	1,174,000	6	B
			After	156.0	842	53.3	0.119			
5	32	M	Before	116.0	680	66.7	0.092	800,000	4	A
			After	24.4	148	11.6	0.022			
6	40	M	Before	105.0	614	82.0	0.081	500,000	—	A
			After	92.0	672	47.3	0.083			

Each value recorded is the average value for three consecutive ten-minute urine collection periods. In the case of Patient 5 the renal blood flow was also determined by renal vein catheterization. Patients 1, 2, and 3 were operated upon during the period of bacitracin administration. Spinal anesthesia was used. Patient 1 had a closure of a colostomy. Patients 2 and 3 had radical dissections of the groins for metastatic disease. Patient 2 received a transfusion without evidence of a reaction.

All values have been corrected to a skin surface area of 1.73 square meters. No corrections have been made for body temperatures because the temperatures of these patients were all between 98° and 99° F.

venous blood. Two different lots of commercially prepared bacitracin were administered to these patients. The lots are identified as lots A and B.

RESULTS

Acute Experiments.—The results of the determinations in the acute experiments are shown in Table I. The values before the administration of bacitracin are the average values of three determinations, and likewise the values for the first half-hour and the second half-hour periods are average values of three determinations done during these periods. No statistically significant changes were observed in the renal functions studied in the acute experiments, since a significant change would be a change greater than the allowed experimental error of plus or minus 10 per cent. However, the

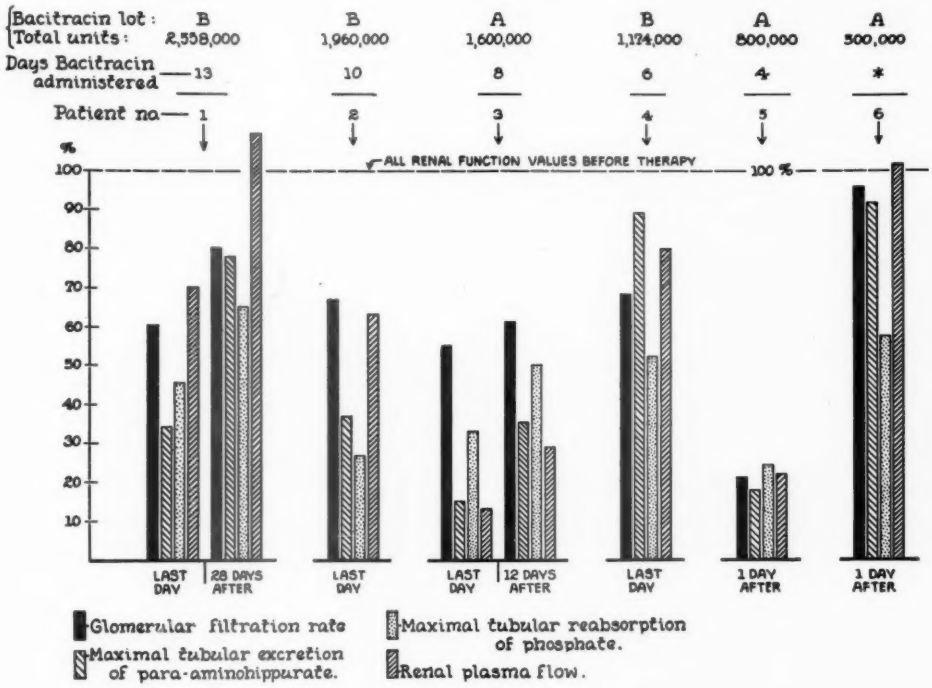

Fig. 1.—Graphic representation of per cent of the various kidney functions remaining after bacitracin therapy as compared to kidney functions before bacitracin therapy in the chronic experiments.

*Patient 6 did not receive bacitracin continuously. He received 150,000 units of bacitracin daily for two consecutive days, none for the next six days, and then 200,000 units in the twenty-four hours preceding the renal function studies shown here.

progressively diminishing values for maximal tubular excretion of para-aminohippurate in Patients 4 and 5 (the only patients in whom this study was done in the acute experiments) are suggestive of early tubular damage. The increases in the filtration fractions from 17.2 to 24.8 per cent and 22.2 and 26.6 per cent, respectively, in Patients 1 and 3 are probably evidences of a slight adrenergic effect and do not represent a diminished ability to secrete para-aminohippurate at the blood concentration employed.

Chronic Experiments.—A moderate to very severe reduction in all of the renal functions studied was observed in all but one of the six patients who had received bacitracin from four to thirteen days. The average values of the

renal functions in the "chronic" experiments are shown in Table II. Each recorded value represents the average of three consecutive observations. Fig. 1 shows the changes in renal function graphically, with the values before bacitracin administration equated to 100 per cent. In the five patients who received the bacitracin without interruption, the decrease in glomerular filtration rate varied from 32 to 79 per cent below the values obtained before bacitracin. Effective renal plasma flow was decreased 20 to 87 per cent; maximum tubular excretion of para-aminohippurate 11 to 85 per cent, and maximal tubular reabsorption of phosphate 48 to 73 per cent. In Patient 5 the effective renal plasma flow was decreased 71 per cent below the value observed before the administration of bacitracin. However, assuming the total renal plasma flow in the patient to be normally 4 per cent greater[11] than the effective renal plasma flow, then the total renal plasma flow after bacitracin was reduced only 50.5 per cent.

DISCUSSION

The maximal secretory or reabsorptive capacity of the renal tubule is an inherent property of the tubular cell and under standard conditions is relatively constant.[2] The decreases in the maximal tubular excretion of para-aminohippurate and of the maximum tubular reabsorption of phosphate represent absolute decreases in renal function. Previous work has demonstrated that as tubular efficiency is impaired the glomerular filtration rate and renal plasma flow also decrease.[12-15]

In the acute experiments the gradual decline of values obtained for maximal tubular excretion of para-aminohippurate in Patients 4 and 5 suggests beginning tubular damage. The variations of maximal tubular reabsorption of phosphate, however, are not uniform throughout the acute experiments. The data suggest that the renal enzyme engaged in the transport of phosphate across the tubular cell is more resistant to the effects of bacitracin than the enzyme involved in the secretion of para-aminohippurate. The early minimal evidences of change in maximal tubular excretion are in accord with the clinical observations since casts and albumin usually do not appear in the urine before the second or third day of parenteral bacitracin therapy.[4]

It has been previously reported that thiosulfate inhibits the antibiotic action of bacitracin.[4] Since bacitracin and sodium thiosulfate were introduced intravenously in the same solution in the acute experiments, it became necessary to determine whether 0.3 mg. per cubic centimeter of sodium thiosulfate would inhibit the activity of 1.2 units per cubic centimeters of bacitracin in the same solution over a period of one hour at room temperature. An aqueous solution containing these concentrations of bacitracin and sodium thiosulfate was allowed to stand at room temperature. At one-, two-, four-, and eight-hour intervals the antibacterial activity of this solution was determined by the plate cup method using a standard strain of *Micrococcus flavus*. The results are compared in Table III with those obtained with an aqueous solution of 1.2 units of bacitracin per cubic centimeter, and with an aqueous solution containing 0.3 mg. per cent sodium thiosulfate. The antibacterial action of

the bacitracin solution and the antibacterial action of the solution of bacitracin and sodium thiosulfate combined were essentially equal. The sodium thiosulfate solution alone had one-half the antibacterial activity of the bacitracin solution as measured directly on the culture media.

TABLE III. ZONES OF INHIBITION OF BACTERIAL GROWTH BY BACITRACIN AND SODIUM THIOSULPHATE AVERAGES OF TRIPLICATE DETERMINATIONS

TIME AT ROOM TEMPERATURE (HR.)	1.2 U PER C.C. OF BACITRACIN ALONE (MM.)	0.33 MG. PER C.C. OF SODIUM THIOSULFATE ALONE (MM.)	BACITRACIN AND SODIUM THIOSULFATE MIXTURE (MM.)
1	19.0	10.5	18.5
2	18.3	10.5	18.0
4	17.3	11.5	16.8
8	17.0	12.0	14.5

From the data obtained it is not possible to state whether any of the bacitracin was actually inhibited. However, the data do indicate that only a small fraction of the bacitracin could have been inhibited in the solution administered.

The reduction in effective renal plasma flow in the "chronic" experiments in Table II and Fig. 1 probably does not indicate similar decrements in total renal plasma flow. In Patient 5 the renal extraction ratio as measured by differences in concentration of para-aminohippuric acid in arterial blood and renal vein blood (by direct catheterization) indicates that only 45.6 per cent of the para-aminohippuric acid was removed in one renal circulation instead of the expected 92 to 96 per cent.[11] Thus, the total renal plasma flow is probably 50 to 60 per cent greater than the effective renal plasma flow after bacitracin. Conversely, the decrement in total renal plasma flow is approximately one-half that in the effective renal plasma flow.

In the chronic experiments the increased volume of glomerular filtrate in relation to tubular function which was consistently observed in the "chronic" experiments indicates that bacitracin predominately affects the tubular epithelium. The data from Patient 6 who received bacitracin for two days, none for the next six days, and then again received bacitracin the day before the renal function tests were repeated, are rather interesting. It would appear that his kidneys had recovered from the effects of the two days of bacitracin administration, and that the marked diminution of tubular excretion of para-aminohippurate was the result of the bacitracin he received in the twenty-four hours immediately preceding the final renal function tests. The data of Patients 1 and 5 probably indicate that relatively few glomeruli continue to function when their tubules become inactive. In Cases 5 the difference between the total renal plasma flow and the effective renal plasma flow represents the volume of plasma perfusing damaged inert renal tissue.

CONCLUSIONS

1. The administration of 23,600 units of commercial bacitracin intravenously, over a period of roughly one hour, caused no statistically signifi-

cant changes in glomerular filtration rate, maximal tubular excretion of para-aminohippurate, or maximal tubular reabsorption of phosphate of renal plasma flow. However, there was a gradual decrease in the average values for maximal tubular excretion of para-aminohippurate which were suggestive of early tubular damage.

2. The commercial bacitracin used in five "chronic" experiments in a dosage of 49,000 to 50,000 units intramuscularly every six hours for four to thirteen days produced moderate to very severe renal damage. The one patient of the "chronic" experimental group who received bacitracin for two days, none for six days, and then again received bacitracin for one day before the renal function tests were repeated, showed marked impairment in tubular excretion of para-aminohippurate but no significant diminution in the remaining renal functions.

3. Two of the five patients of the chronic experimental group showed evidences of considerable recovery of the renal functions studied, twelve days and twenty-eight days after bacitracin was discontinued.

4. The data indicate that bacitracin predominantly affects the tubular epithelium.

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LOCAL REACTION TO OXIDIZED CELLULOSE AND GELATIN HEMOSTATIC AGENTS IN EXPERIMENTALLY CONTAMINATED RENAL WOUNDS

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EXPERIENCE with patients in whom abscesses formed in renal wounds after the use of Oxycel* for bolsters and for hemostasis led us to doubt the reports of the benign nature of this foreign substance. Then MacDonald and Matthews in 1947 published their study of absorbable hemostatics in experimental nephrotomy incisions with the conclusion that these substances were easily and rapidly absorbed. We felt, however, that their conclusions were not applicable to clinical urology because such incisions are seldom made in uninfected kidneys but are usually made for stone, obstruction, or focal infection. We, therefore, began a series of experiments to compare the healing of contaminated renal wounds which were packed with absorbable hemostatic with similar wounds not packed.

MATERIALS AND METHODS

Young rabbits were chosen because of their known resistance to adventitiously introduced infection and because of their availability. After preoperative administration of atropine, anesthesia was obtained with drop ether. The lumbar approach to the kidneys was used (Fig. 1, *a*) and the right side was closed before the left incision was made. The right kidney was lifted into the wound, the edges of which were protected by gauze packs. A long coronal nephrotomy incision was made from pole to pole extending approximately halfway to the pelvis; the calyx was not purposely entered. Brisk bleeding was invariably encountered. A piece of Gelfoam† 3 by 2 by 1.5 cm. or folded Oxycel of the same general dimensions was inserted into the wound and two mattress sutures of 0000 chromic catgut swedged on cutting-edge needles were placed in the capsule such that hemostasis was effected (Fig. 1, *b*). Using a blunted 22 gauge needle, 0.1 c.c. of dilute autogenous fecal suspension was injected beneath the pack. The flank wound was closed with continuous cotton sutures. A similar procedure was done on the left side except that hemostasis was secured by the two mattress sutures without packing; an equal amount of fecal suspension was injected. The animals were then killed by decapitation at selected intervals (from three days to three weeks), and autopsy was performed after preparing the abdomen as for the original operation. Through separate incisions, each kidney and an adjacent portion of the body musculature was removed with sterile technique. Section (Fig. 1, *c*) was made in each kidney at right angles to the nephrotomy incision, so that smears, cultures, and photographs could be

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†Gelfoam was provided through the generosity of The Upjohn Company, Kalamazoo, Mich.

made before the specimen was fixed in 10 per cent formalin. Serial hand sections were then cut and the most altered portions sent for imbedding, sectioning, and staining with hematoxylin and eosin.

RESULTS

Thirty-nine rabbits were operated upon (Table I). Of these, 2 died spontaneously and when discovered were too autolysed for study. Of the remaining 37, 23 had a gross abscess in the right (treated) nephrotomy incision and no abscess on the left. Seven had abscesses on the right and in addition had a healing infarcted area on the left which lacked acute inflammatory response. Four had abscesses on the left which were smaller than those on the packed side and 2 had larger ones on the left. In one animal (twenty-one days) neither side contained an abscess.

The first and largest group, consisting of 23 animals, was Group A (Table I) in which the abscess developed only on the right. The photograph (Fig. 2) shows a typical result (Rabbit 15, Gelfoam pack, killed at fourteen days): a

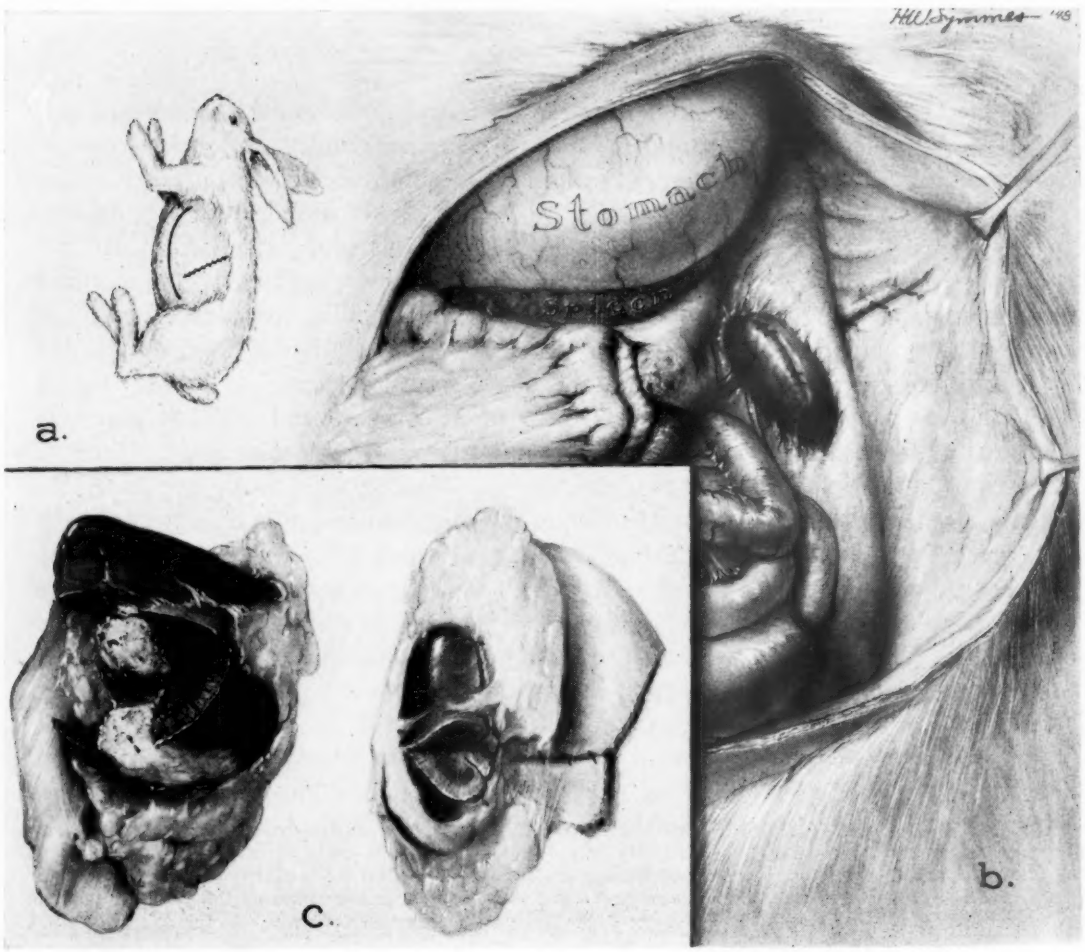

Fig. 1.—*a*, Operative incision (oblique) and autopsy incision (curved). *b*, Unpacked (left) kidney in situ. *c*, Right and left kidneys opened transversely showing abscess on right, scar of incision on left. (Rabbit 4, Gelfoam pack, killed after fourteen days.)

large abscess filled with creamy pus in the right kidney (*a*) and a thin white line marking the line of the incision on the left (*a'*). Cultures showed nonhemolytic *Staphylococcus albus* bilaterally. As seen on the low-power (*b*) and high-power (*c*) photomicrographs, the right kidney is involved in an acute inflammatory process, with abscess formation. Five zones are distinguished: compressed renal tissue, dilated tubular area, fibrous barrier, pus, and involved Gelfoam—in that order from outside in. On the left (*b'*, *c'*), on the contrary, there is a thin line of repair tissue without inflammation. A similar result (Fig. 3) was found in Rabbit 35, killed at fourteen days. In 21 other cases similar changes were found.

TABLE I. RELATION OF INCIDENCE OF ABSCESS TO PRESENCE OF HEMOSTATIC AGENT

GROUP DESCRIPTION	SITE OF ABSCESS: RIGHT (PACKED) KIDNEY	SITE OF ABSCESS: LEFT (UNPACKED) KIDNEY	TOTAL ANIMALS	PERCENTAGE IN GROUPS
A Right abscess, left negative	23	0	23	63.9 19.4 } 83.3
B Right abscess, left infarcted area	7	0 (infarction in 7)	7	
C Bilateral abscesses	6	6	6	16.7

A second group (Group B, Table I) is made up of those animals with a well-developed abscess on the right and with a zone of infarction about the line of incision on the left. Rabbit 33 (Oxycel pack, killed at fourteen days) is characteristic. The photograph (Fig. 4) shows the large pus-filled abscess and hematoma on the right (*a*) and the smaller pale infarcted area on the left (*a'*). Microscopic sections show the great polymorphonuclear cell reaction about the right abscess (*b* and *c*) and the almost complete absence of acute inflammatory reaction in the infarcted area on the left (*b'* and *c'*). The detail of this intense polymorphonuclear cell response on the right is seen in *d*, while faded autolysed cells without inflammatory reaction are found in *d'*. Essentially this same picture was seen in the remaining 6 cases of this group and was doubtless due to severance of the blood supply by the incision.

One other group must be mentioned (Group C, Table I). In 4 cases, acute inflammatory reaction with abscess formation took place on both sides, and in 2 cases it was more severe on the left than on the right. The interpretation is that an overwhelming dosage of organisms was administered followed by infarction or hematoma formation.

There was little to differentiate the effects of Gelfoam and Oxycel, nor did breakdown into duration before autopsy show significant differences (Table II). The rather high percentage of positive cultures on the untreated side (Table III) indicates that in many unpacked incisions tissue infection was present but since it was being handled by the local defense mechanisms without hindrance by foreign material, accumulation of bacteria and pus did not occur. Analysis of infecting organisms gave no indication that any particular bacterium increases the likelihood of abscess formation about the pack (Table IV). Mixed infections occurred in 22 kidneys.

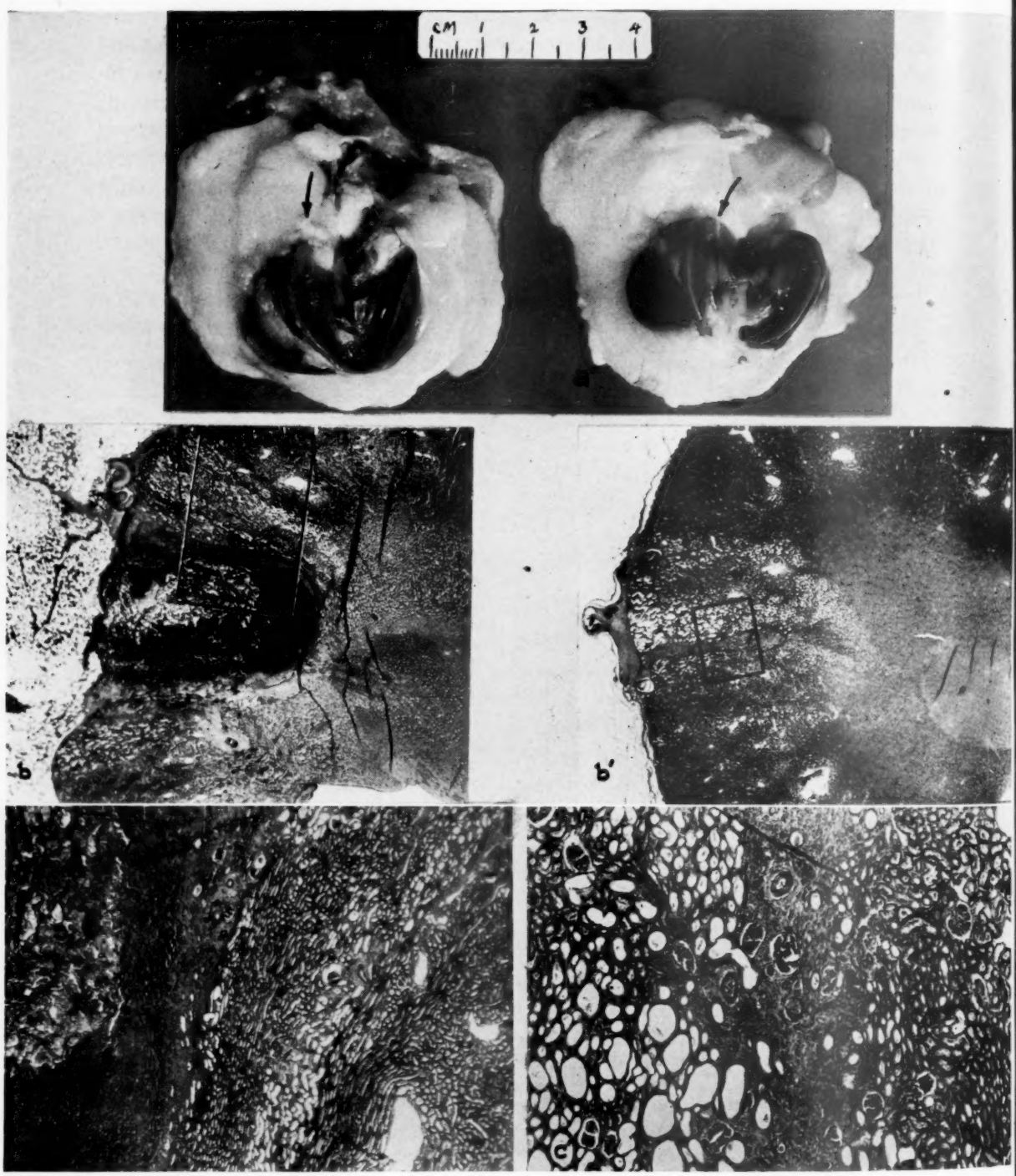

Fig. 2.—*a*, Right kidney with abscess; *a'*, left kidney with fine white line of healing incision. *b*, Cross section of right incision with abscess (×5); *b*,' cross section of left incision (×5). *c*, Detail of *b*, showing interstices of Gelfoam filled with pus (×30); *c'*, detail of *b'*, showing healing scar (×45). (Rabbit 15, Gelfoam pack, killed after fourteen days.)

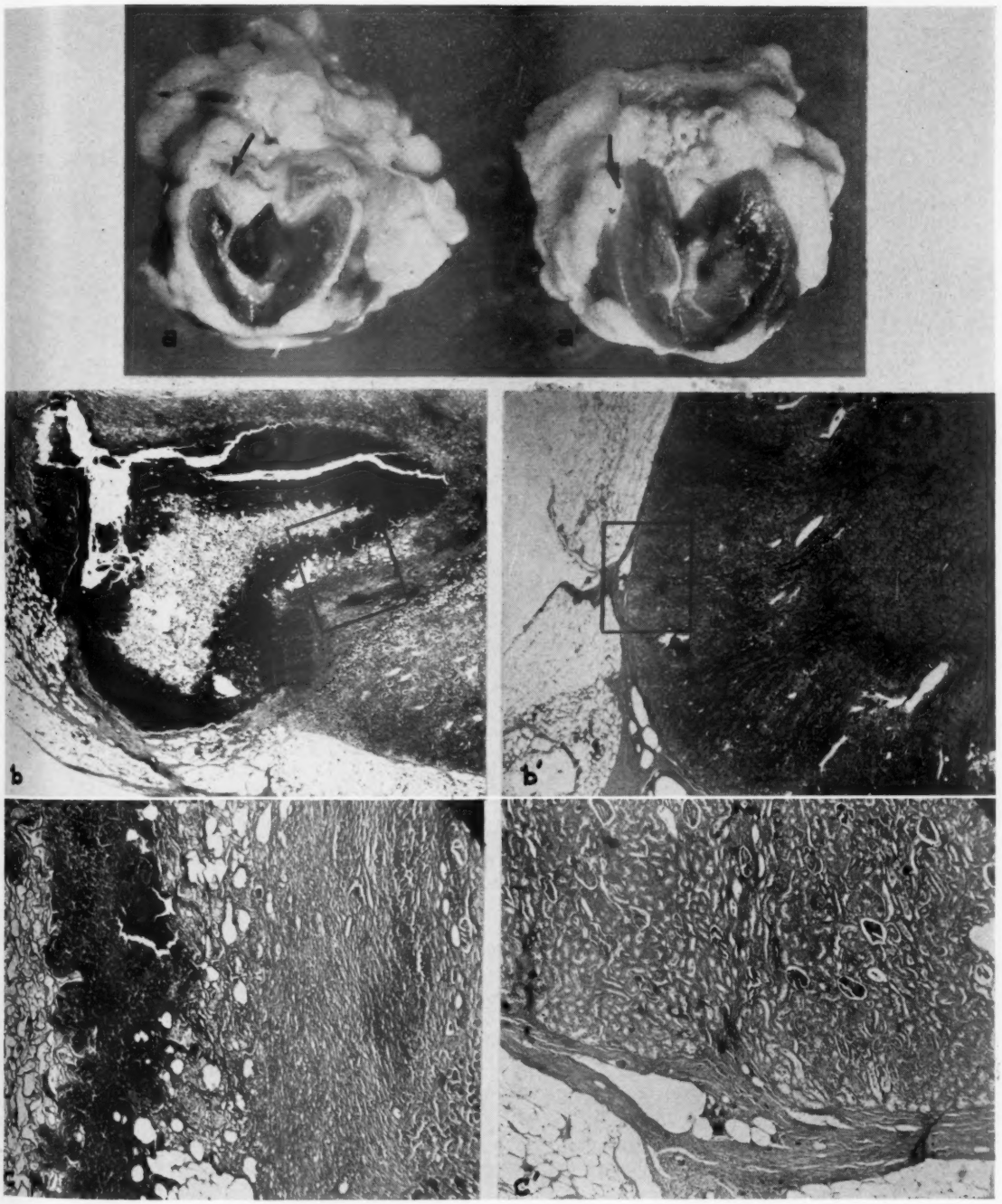

Fig. 3.—*a*, Right kidney with abscess; *a'*, left kidney with healing incision, similar to Fig. 2; *b* and *b'* (×5) cross sections of wound; *c* and *c'* (×45) detail of *a* and *b*. (Rabbit 35, Gelfoam pack, killed at fourteen days.)

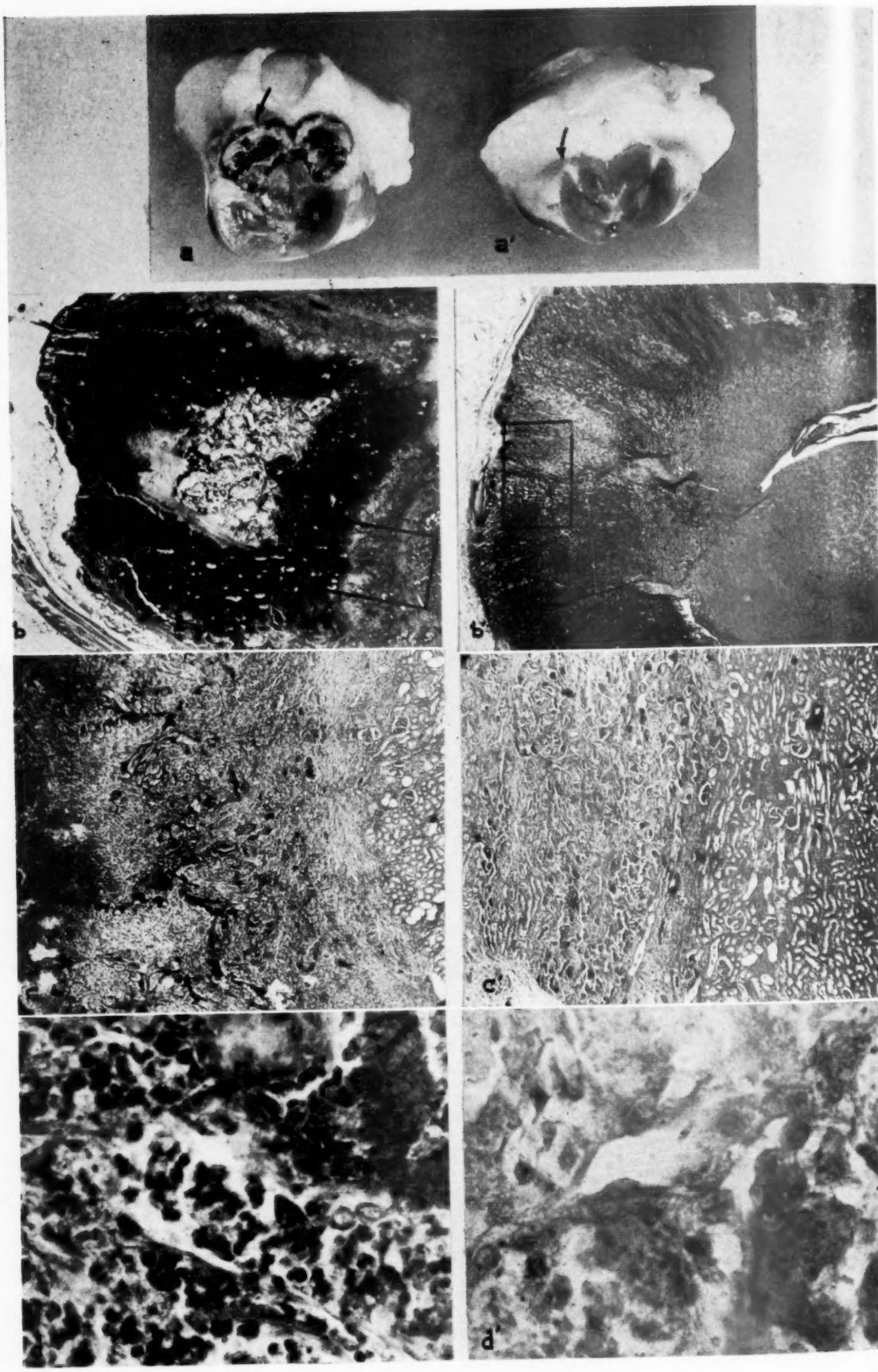

Fig. 4.—(*For legend see opposite page.*)

TABLE II. INCIDENCE OF ABSCESS IN RELATION TO TYPE OF HEMOSTATIC AGENT, AND TO DURATION OF INFECTION

DAYS	ABSCESS ON PACKED SIDE ONLY		BILATERAL ABSCESSES	
	GELFOAM	OXYCEL	GELFOAM	OXYCEL
3 to 5	2	1		
7	2	5	2	
14	8	7		4
21	3	2		
Total cases	15	15	2	4

TABLE III. INCIDENCE OF POSITIVE CULTURES IN RIGHT (PACKED) AND LEFT (UNPACKED) KIDNEYS

	RIGHT	LEFT
Growth	84% (31 cases)	59% (22 cases)
No growth	16% (6 cases)	41% (15 cases)

TABLE IV. INFECTING ORGANISMS BY GROUP

BACTERIA (IN ORDER OF FREQUENCY)	GROUP A (23 CASES)		GROUP B (7 CASES)		GROUP C (6 CASES)	
Escherichia coli	5	5	2	1	3	1
Nonhemolytic Staphylococcus albus	4	3	2	2	2	2
Streptococcus fecalis	5	2	1	0	2	1
Clostridia	2	4	1	0	1	1
Alpha Streptococcus	2	1	1	2	0	0
Diphtheroids	2	2	1	0	2	0
Beta Streptococcus	2	0	0	0	1	0
Staphylococcus aureus	2	0	1	1	0	0
Gamma Streptococcus	2	0	1	0	0	0
Proteus vulgaris	0	1	0	0	0	0
Pseudomonas aeruginosa	0	1	0	0	0	0
Hemolytic Staphylococcus albus	1	0	0	0	0	0
Anaerobic Streptococcus	0	1	0	0	0	0

DISCUSSION

Statistically significant conclusions are reached which confirm good surgical teaching: that any foreign body, however nonreactive and absorbable, is detrimental to wound healing especially in the presence of infection. Although Jenkins and co-workers had warned that bulky gelatin sponges may become rapidly liquefied and offer a culture medium which may influence the development of infection, and others (Uihlein and co-workers, Goldstein and Hollander, and Merricks) felt that large amounts should be avoided, most workers found no contraindication to the use of these substances in contaminated wounds. The strongest warning came recently when Laufman and Method demonstrated experimentally the adverse effect of absorbable hemostatic agents in bowel anastomosis. The present study confirms the opinions of those who would limit the use of these substances in the presence of infection.

SUMMARY

To test the reactivity of absorbable hemostatic agents in contaminated wounds, 39 rabbits were subjected to extensive bilateral nephrotomy incisions,

Fig. 4.—*a*, Right kidney with abscess; *a'*, left kidney with pale infarct; b and *b'*, cross sections of wounds (×5); *c* and *c'*, detail of above sections *a* and *b* (×45); *d* and *d'*, cellular detail of *a*, *b*, and *c* (×460) showing dense polymorphonuclear cell reaction on the right and vague autolysed tubular cells on the left, without inflammatory reaction. (Rabbit 33, Oxycel pack, killed at fourteen days.)

contaminated with a suspension of autogenous feces. The right incision in each animal was closed over an Oxycel or Gelfoam pack; the left was merely closed.

Abscesses were almost constantly found in the right (packed) kidney (in 36 of 37 animals), and infrequently found on the left (unpacked) side (6 of 37 animals). Two rabbits were discarded because of post-mortem autolysis, and one showed bilateral healing.

The interpretation is made that these agents should be used sparingly in clinical nephrotomy incisions and at other sites in urologic surgery since such wounds are commonly contaminated by infected urine.

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SPONTANEOUS EXTERNAL BILIARY FISTULAS

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A SPONTANEOUS external biliary fistula was observed recently which opened through the abdominal wall in the midline above the umbilicus. Because of the rarity of this type of fistula it is reported with a brief review of the literature.

CASE REPORT

History.—M. P., an obese white woman, aged 72 years, was admitted to the University of Kansas Medical Center, Nov. 4, 1947, complaining of an opening in the abdominal wall which had been present one and one-half years. The patient first noticed a painless, soft, round swelling in the midline approximately two inches above the umbilicus. This swelling gradually increased in size, became more superficial, and after three months ruptured to the outside spontaneously, discharging a yellowish pus which was nonirritating and essentially odorless. The quantity of drainage was rather copious at first but it soon decreased, persisting as only a slight constant ooze.

Physical Examination.—There was an opening in the midline of the abdomen 3 to 4 mm. in diameter, located 5 cm. above the umbilicus. From the opening, which had the appearance of a sinus, small quantities of yellow, purulent material could be expressed. A small paraumbilical hernia was present. This hernia was easily reducible. The blood pressure was 170 systolic and 80 diastolic. The remainder of the physical examination was within normal limits for a woman of 72 years of age. A scout film of the abdomen revealed an irregular area of increased density, measuring 3 by 4 cm., which was constant in size, shape, and position with that of a calcified gall bladder. X-ray studies showed a normal gastrointestinal tract. Lipiodol injection of the sinus tract permitted a more complete visualization of the calcified structure in the upper right quadrant. The lipiodol passed into the intestine (Fig. 1). It was the roentgenologist's opinion that the dye entered the duodenum. A diagnosis of biliary fistula was made.

Operative Note.—A right transrectus incision was made near the midline above the level of the umbilicus. The gall bladder was partially calcified and filled with stones. Extending from the fundus of the gall bladder there was a fistulous tract which passed through the fat of the falciform ligament, to and through the abdominal wall in the midline. The common duct and the common hepatic duct were stretched and angulated to form an inverted V (Fig. 2). There was an anomalous right hepatic artery which lay near the cystic duct. The gall bladder was removed and the paraumbilical hernia was repaired through the abdominal incision.

The pathologist's report was acute and chronic fibrous cholecystitis and pericholecystitis with calcification, cholelithiasis, and chronic periportal hepatitis.

Thilesus, in 1670,[1] is generally credited with reporting the first case of biliary fistula due to perforation of gallstones through the abdominal wall. In 1890 Courvoisier[2] published a collection of 499 cases of perforation of the gall bladder, 169 of which were listed as spontaneous fistulas through the abdominal wall. Naunyn[3] recorded 184 cases in 1896, and in 1897 Bonnet[4] collected 122 cases. Since the reviews of Naunyn and Bonnet indicated that some of the diagnoses were founded upon clinical impressions and not proved by operation or autopsy, we have accepted Courvoisier's summary as probably most accurate and have added case reports from 1890 to June, 1948 (Tables I and II).

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Spontaneous biliary fistula usually arises as a result of gallstones and suppurative cholecystitis. Inflammatory adhesions form between the gall bladder fundus and the abdominal parietes. A perforation at the point of contact discharges pus within the substance of the abdominal wall, forming an abscess. At length the abscess burrows through the skin, establishing communication between the fundus and the exterior. Long fistulous tracts may develop within the abdomen and eventually perforate through the skin. These

Fig. 1.—Radiograph showing tube in sinus tract with contrast medium in gall bladder, common bile duct, and duodenum.

fistulas usually arise from the fundus of the gall bladder rather than from one of the ducts. It is not uncommon to find that the perforation in the gall bladder wall has become sealed after expulsion of pus and stones through the abdominal wall, and a sinus tract persists.

After a review of the literature it becomes apparent that prior to the advent of surgical intervention as the treatment of cholecystitis, the incidence of such complications as suppuration and empyema of the gall bladder with

subsequent perforation and fistula formation was much higher. This, at present, seems the best explanation of the greater number of cases collected in earlier years.

TABLE I. LOCATIONS OF PERFORATIONS

COURVOISIER			CASES SINCE 1890	
Im r. Hypochondrium	49	85	Rt. upper quad.	11
Am Rand der r. Rippenbogen	36			
Im r. Mesogastrium	17	27	Rt. lower quad.	4
Im r. Regio iliaca	10			
Im Epigastrium	6	6	Epigastrium	0
In der Nahe des Nabels	26	38	Umbilicus and region of umbilicus	12
Im Nabel	12			
Unter dem Nabel	11	11	Below umbilicus	4
In linker Leiste	1	1	Left flank	2
Multiple	1	1	Multiple	1
			Rt. flank	1
			Rt. thigh	2
		169		37

Spontaneous external biliary fistula, as a complication of cholecystitis, is chiefly a disease of women of the older age group in the fifth to seventh decades. This predilection for women is unquestionably a reflection of the higher incidence of cholecystitis in women as compared with men.

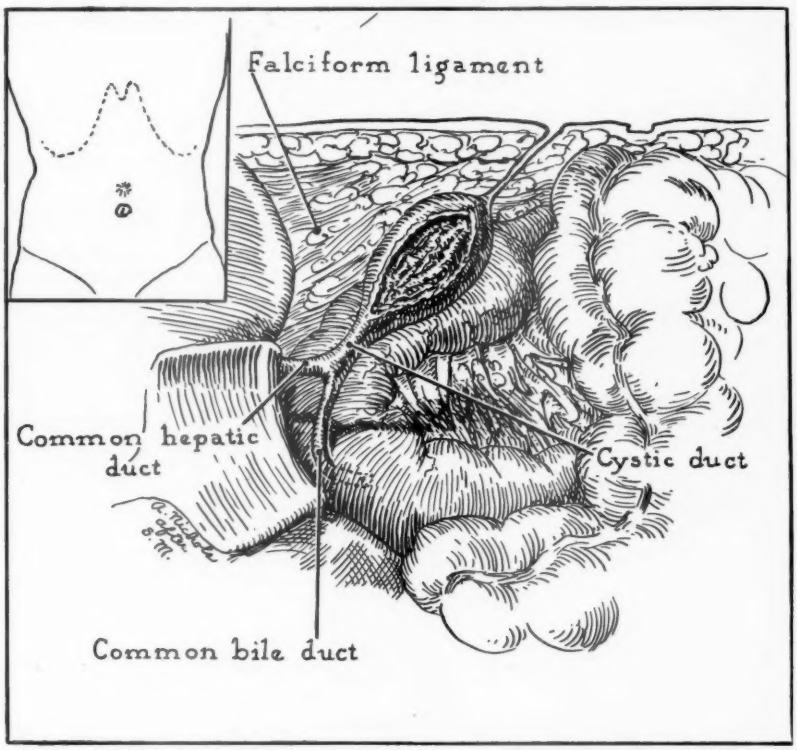

Fig. 2.—Sketch showing gall bladder, bile ducts, and sinus tract to abdominal wall. Location of fistula opening is shown in inset.

The fistulous site, usually single, is found most frequently in the right upper quadrant of the abdominal wall. In certain cases the fistula has been directed by the falciform ligament to the region of the umbilicus in the midline. Other more distant points of fistulous openings in the abdominal wall

TABLE II. LIST OF PUBLISHED CASES OF SPONTANEOUS EXTERNAL PERFORATION OF THE GALL BLADDER SINCE 1890

AUTHOR	YEAR	AGE	SEX	LOCATION	STONE	COLIC	RESULT
Oppenheim[5]	1890	69	F	Rt. lower quad.	Yes	Yes	Persistent
Taylor[6]	1890	60	F	1 inch below umbilicus	Yes	Yes	Persistent
Colegrove[7]	1891	83	F	Umbilicus	Yes	Yes	Spont. healing
Knoop[8]	1892	32	F	Below umbilicus	Yes	Yes	Incision and drainage with spont. healing
		62	F	Above umbilicus	Yes	Yes	Incision and drainage with spont. healing
Guepin[9]	1894	76	F	Rt. hypochond.	Yes	No	Spont. healing
Bonnet[4]	1897	50	F	Rt. subcostal	Yes	No	Spont. healing
Trille[10]	1899	?	F	Left flank	No	Yes	Persistent
Fabricius[11]	1899	60	F	Umbilicus	Yes	No	Persistent
		40	F	Rt. hypochond.	Yes	No	Excision and healing
Porges[12]	1900	47	F	Rt. thigh	Yes	Yes	Excision and healing
Gibbon[13]	1901	50	F	Umbilicus	Yes	Yes	Excision and drainage with healing
Pinatelle and Horand[14]	1906	53	F	Rt. iliac fossa	Yes	Yes	Persistent
Abell[15]	1909	23	M	Rt. thigh	Yes	No	Excision and healing
Vignard[16]	1909	60	F	Rt. lower quad.	Yes	Yes	Incision and drainage with healing
Tisserand[17]	1910	65	F	Umbilicus	Yes	Yes	Spont. healing
Patel and Cotte[18]	1910	37	F	Umbilicus	Yes	Yes	Cholecystectomy with excision and healing
Beje[19]	1915	57	?	Rt. flank	Yes	Yes	Not reported
Horhammer[20]	1916	38	F	Rt. hypochond.	Yes	Yes	Excision with healing
Dyas[21]	1920	44	F	Near umbilicus	Yes	Yes	Excision with healing
Lammert[22]	1922	67	F	Rt. hypochond.	Yes	Yes	Not reported
Georg[23]	1925	56	F	Rt. subcostal	Yes	Yes	Not reported
Zhvanetzky-Zabolotnyi[24]	1928	27	F	Near umbilicus	Yes	Yes	Cholecystectomy with excision and healing
Gariepy[25]	1929	51	F	Rt. subcostal 2—hypochond.	Yes	Yes	Not reported
Davis[26]	1930	60	F	Multiple (1—epigastrium)	Yes	Yes	Spont. healing
McCay[27]	1930	74	F	Left lumbar	Yes	Yes	Cholecystectomy with excision and healing
Salisachs[28]	1932	64	M	Rt. hypochond.	Yes	Yes	Persistent
Gill[29]	1934	74	F	Below umbilicus	Yes	Yes	Excision and healing
Adams[30]	1934	55	F	Hypochond.	Yes	Yes	Spont. healing
Walzel[31]	1937	54	F	Umbilicus	Yes	Yes	Excision and healing
Begnis[32]	1938	40	?	Rt. iliac fossa	Yes	Yes	Persistent
Moschl[33]	1939	75	M	Above umbilicus	Yes	No	Persistent
Michans and Mugaburn[34]	1941	54	F	Umbilicus	Yes	Yes	Not reported
Rankin et al.[35]	1942	78	M	Rt. subcostal	Yes	Yes	Persistent
Piulachs and Pelazo[36]	1944	50	F	Below umbilicus	Yes	Yes	Excision and healing
Scarpa[37]	1945	52	M	Rt. hypochond.	Yes	Yes	Persistent
Henry and Orr	1948	72	F	Above umbilicus in midline	Yes	No	Cholecystectomy with excision and healing

have been reported; for example, right iliac fossa (Gibbon[13]), and right thigh (Porges,[12] Abell[15]). Multiple fistulas may occur (Fig. 3).

The nature of the discharge from the fistulas varies. Often the cystic duct has been obliterated by a stone, and only pus or viscid mucus will be emitted. In other cases, the cystic duct may be patent and bile may or may not flow from the fistulous orifice. Calculi are present in nearly all cases, and a history of previous biliary colic is the rule. The passage of many small stones or a solitary large stone is not uncommon.

In those instances where lipiodol injection of the fistulous tract was attempted, a partial visualization of the biliary ducts and first portion of the duodenum was obtained. This procedure is recommmended as a reliable preoperative diagnostic aid, but its efficacy is obviously dependent upon the patency of the cystic duct.

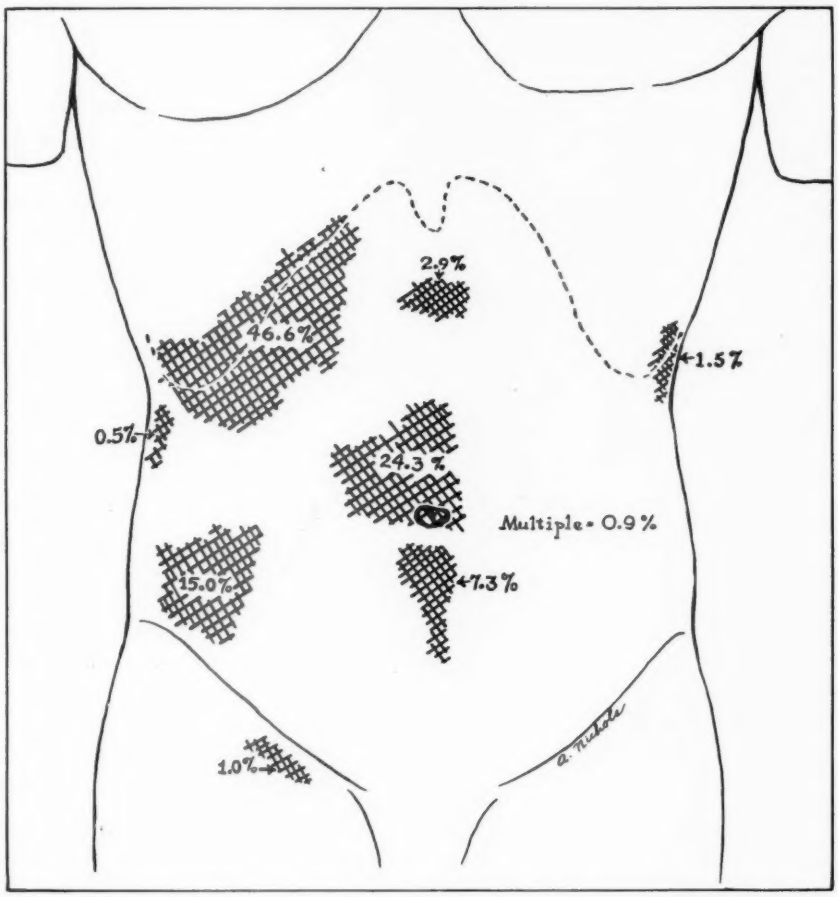

Fig. 3.—Sketch showing locations of 206 external biliary fistulas in percentages of total number.

After expulsion of calculi, or their extraction by suitable operative procedures, many fistulas have healed spontaneously. The present-day treatment, that of cholecystectomy with excision of the tract in its entirety, is the therapy of choice.

SUMMARY

A case of spontaneous perforation of the gall bladder through the midline of the abdominal wall is reported. A total of 205 cases of external biliary fistula have been found in the literature, 36 of which have been recorded since 1890.

Spontaneous external biliary fistulas are rare. It is probable that such fistulas were more common before cholecystostomy and cholecystectomy became the accepted treatment of gall bladder disease.

Early literature on abdominal biliary fistulas is somewhat confusing, because of inaccuracies of diagnosis.

The unusual findings in the case here reported were: (1) calcification of the gall bladder, (2) elongation and angulation of the common hepatic and common bile ducts, and (3) a tortuous fistulous tract which passed from the fundus of the gall bladder through the fat of the falciform ligament and midline of the abdominal wall above the umbilicus.

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HORMONE PREPARATIONS IN THE TREATMENT OF TWO HUNDRED EIGHTY-TWO MANN-WILLIAMSON DOGS

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INTRODUCTION

THE relation of hormones to peptic ulcer is suggested by the following: Peptic ulcer and its complications are less common in women than in men;[1, 2] with the onset of pregnancy, ulcer symptoms as a rule disappear;[3, 4] and active peptic ulcer is extremely rare during pregnancy.[3, 4, 5] The sex incidence of peptic ulcer in children before puberty shows a ratio of 1:1, but as the child approaches maturity the incidence is higher in the male.[6] Peptic ulcer, not infrequently, has its onset during the climacterium,[1] and the symptoms of peptic ulcer are aggravated during the menopause.[4] We have found also in a study of thirty women with proved duodenal ulcer that 47 per cent showed an endocrine imbalance (exclusive of menopause).[4] It was felt, therefore, that perhaps the normal female may be protected against peptic ulcer by some inherent mechanism peculiar to her sex; that a normal reproductive cycle and the increased glandular activity during active sex life and pregnancy probably serve to prevent duodenal ulcers.[7] This naturally suggested the possibility that protection might in some way depend on hormones. We have accordingly attempted to study this question by administering various hormone preparations to dogs with the experimentally produced Mann-Williamson ulcers.

THE MANN-WILLIAMSON ULCER

The Mann-Williamson ulcer[8, 9] is a surgically produced ulcer. The pylorus is anastomosed to the jejunum 15 to 20 cm. distal to the ligament of Treitz. The duodenum is detoured into the terminal ileum about 25 cm. proximal to the ileocecal junction. A chronic ulcer nearly always develops in the jejunum opposite the stoma. Grossly and microscopically it is analogous to the postoperative jejunal ulcer following gastroenterostomy in the human being. All of our control animals died with ulcer within 135 days of the operation, with an average survival of 63 days. All the layers of the intestinal wall were involved. Of the untreated animals, 75 per cent died of peritonitis following perforation of the ulcers. There was very little attempt at healing.

METHOD OF STUDY

All animals were fed a diet consisting of hospital leftover foods, principally meats, with no supplements. This diet differs from the one used by Ivy[10] in that Ivy and his associates used commercial dog food plus fresh ground raw hog pancreas, fresh ground raw hog liver, and whole milk. We did not use this special diet because our control animals did not receive it.

Ten different series of Mann-Williamson dogs were treated parenterally. Three additional series were treated orally. (See Chart 1.) The dosage of each preparation is noted on the chart. Treatment was begun on the third or

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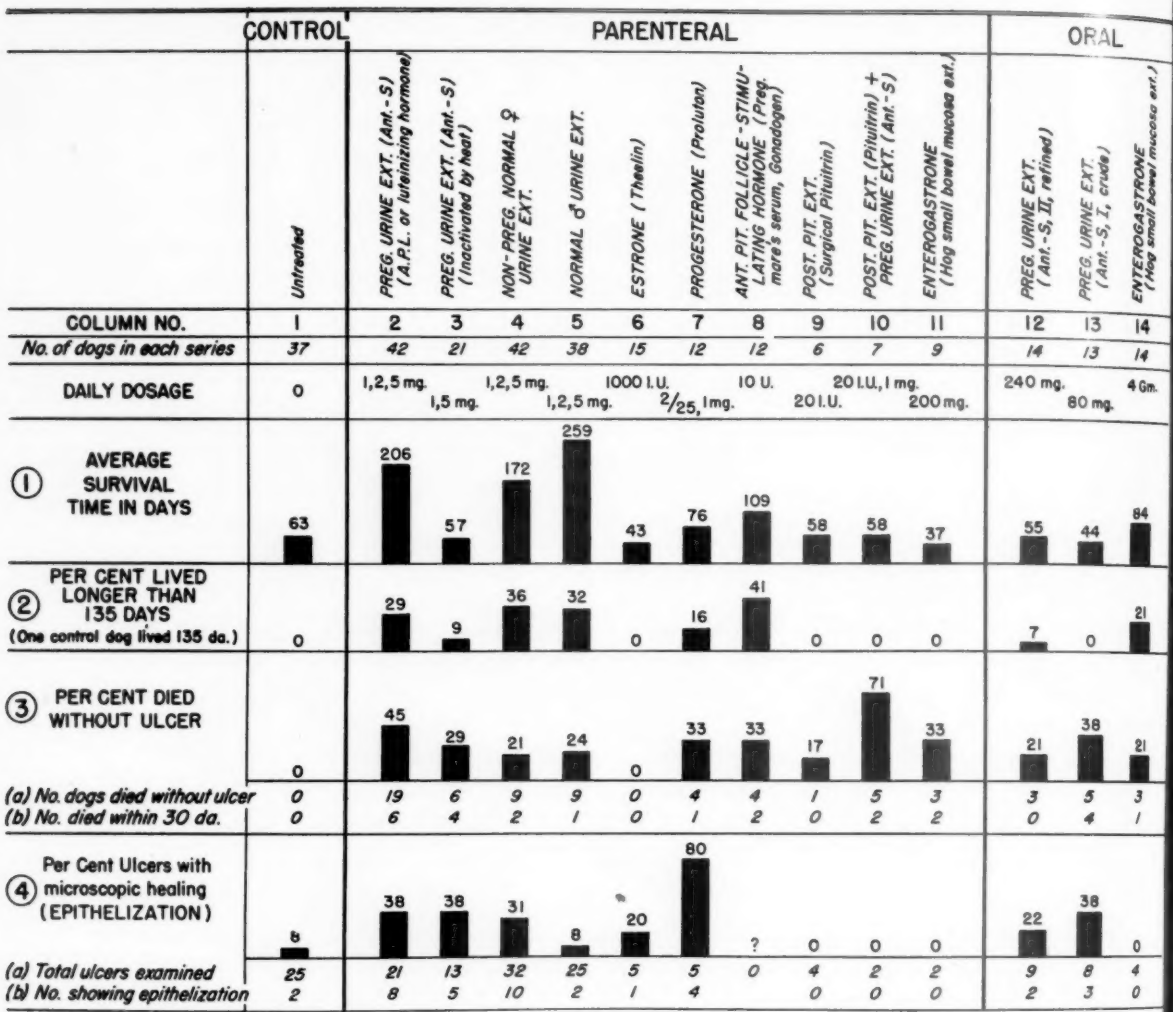
CONTROL
PARENTERAL
ORAL
Untreated
PREG. URINE EXT. (Ant.-S) (A.P.L. or luteinizing hormone)
PREG. URINE EXT. (Ant.-S) (Inactivated by heat)
NON-PREG. NORMAL ♀ URINE EXT.
NORMAL ♂ URINE EXT.
ESTRONE (Theelin)
PROGESTERONE (Proluton)
ANT. PIT. FOLLICLE-STIMULATING HORMONE (Preg. mare's serum, Gonadogen)
POST. PIT. EXT. (Surgical Pituitrin)
POST. PIT. EXT. (Pituitrin) + PREG. URINE EXT. (Ant.-S)
ENTEROGASTRONE (Hog small bowel mucosa ext.)
PREG. URINE EXT. (Ant.-S, II, refined)
PREG. URINE EXT. (Ant.-S, I, crude)
ENTEROGASTRONE (Hog small bowel mucosa ext.)
COLUMN NO.
No. of dogs in each series
DAILY DOSAGE
1,2,5 mg.
1,5 mg.
1,2,5 mg.
1,2,5 mg.
1000 I.U.
2/25, 1 mg.
10 U.
20 I.U., 1 mg.
20 I.U.
200 mg.
240 mg.
80 mg.
4 Gm.
① AVERAGE SURVIVAL TIME IN DAYS
② PER CENT LIVED LONGER THAN 135 DAYS (One control dog lived 135 da.)
③ PER CENT DIED WITHOUT ULCER
(a) No. dogs died without ulcer
(b) No. died within 30 da.
④ Per Cent Ulcers with microscopic healing (EPITHELIZATION)
(a) Total ulcers examined
(b) No. showing epithelization

	Untreated	PREG. URINE EXT. (Ant.-S) (A.P.L. or luteinizing hormone)	PREG. URINE EXT. (Ant.-S) (Inactivated by heat)	NON-PREG. NORMAL ♀ URINE EXT.	NORMAL ♂ URINE EXT.	ESTRONE (Theelin)	PROGESTERONE (Proluton)	ANT. PIT. FOLLICLE-STIMULATING HORMONE (Preg. mare's serum, Gonadogen)	POST. PIT. EXT. (Surgical Pituitrin)	POST. PIT. EXT. (Pituitrin) + PREG. URINE EXT. (Ant.-S)	ENTEROGASTRONE (Hog small bowel mucosa ext.)	PREG. URINE EXT. (Ant.-S, II, refined)	PREG. URINE EXT. (Ant.-S, I, crude)	ENTEROGASTRONE (Hog small bowel mucosa ext.)
COLUMN NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14
No. of dogs in each series	37	42	21	42	38	15	12	12	6	7	9	14	13	14
DAILY DOSAGE	0	1,2,5 mg.	1,5 mg.	1,2,5 mg.	1,2,5 mg.	1000 I.U.	2/25, 1 mg.	10 U.	20 I.U.	20 I.U., 1 mg.	200 mg.	240 mg.	80 mg.	4 Gm.
① AVERAGE SURVIVAL TIME IN DAYS	63	206	57	172	259	43	76	109	58	58	37	55	44	84
② PER CENT LIVED LONGER THAN 135 DAYS (One control dog lived 135 da.)	0	29	9	36	32	0	16	41	0	0	0	7	0	21
③ PER CENT DIED WITHOUT ULCER	0	45	29	21	24	0	33	33	17	71	33	21	38	21
(a) No. dogs died without ulcer	0	19	6	9	9	0	4	4	1	5	3	3	5	3
(b) No. died within 30 da.	0	6	4	2	1	0	1	2	0	2	2	0	4	1
④ Per Cent Ulcers with microscopic healing (EPITHELIZATION)	8	38	38	31	8	20	80	?	0	0	0	22	38	0
(a) Total ulcers examined	25	21	13	32	25	5	5	0	4	2	2	9	8	4
(b) No. showing epithelization	2	8	5	10	2	1	4		0	0	0	2	3	0

Chart 1.—Hormone preparations in the treatment of 282 Mann-Williamson dogs.

fourth postoperative day and was continued daily until the animal died. Death usually was due either to inanition or to peritonitis, following perforation of the ulcer.

Ten of the thirteen series were treated with hormone preparations associated with the female reproductive cycle. These are:

1. The anterior pituitary-like or luteinizing hormone prepared from human pregnancy urine—(Ant-S., Parke Davis & Co.). One series was treated parenterally and two series were treated orally. Another series was treated parenterally with a combination of A.P.L. hormone (Ant-S) and posterior pituitary extract (Surgical Pituitrin).
2. A heat inactivated pregnancy urine extract (Ant-S heated for four hours at 90 to 95° C.).
3. Estrone (Theelin—Parke Davis & Co.).
4. Progesterone (Proluton—Schering Corp.).
5. The anterior-pituitary follicle-stimulating hormone prepared from pregnant mare's serum (Gonadogen—Upjohn & Co.).

6. Two series of animals were each treated parenterally either with an extract prepared from urine of normal (non-pregnant) women or with an extract of urine from normal men. These two extracts were prepared by the method of Katzman and Doisy,[11] which was used in the preparation of commercial pregnancy urine extract (Ant.-S). The urine of both normal (nonpregnant) women and that of normal men contains varying quantities of the anterior-pituitary follicle-stimulating hormone, estrogens and androgens.

Investigations of hormone factors not related to the reproductive system have been limited to (1) the posterior pituitary factors (Surgical Pituitrin) and (2) enterogastrone (an extract prepared from the mucosa of the small bowel of the hog). With enterogastrone one series was treated parenterally and another orally.

The therapeutic efficacy of these hormone preparations was determined by the following four criteria:

1. Comparing the average survival time of the treated animals with that of untreated controls. The 37 untreated animals lived, on the average, 63 days after the Mann-Williamson operation.

2. Determining the percentage of treated animals that lived longer than the maximum survival time of the untreated animals. The maximum survival time of the untreated dogs was 135 days (one animal).

3. Comparing the percentage of the animals that died without ulcer in the different series. All animals in the untreated series died with the typical jejunal ulcers.

4. Comparing the percentage of ulcers in the different groups showing microscopic evidence of epithelization. Of the 25 ulcers in the untreated series examined microscopically, 2 (or 8 per cent) showed epithelization.

RESULTS

It will be noted from Chart 1 that:

1. The average survival time was appreciably increased in the series of animals treated parenterally with:

   (a) the urine extract prepared from normal men (259 days)
   (b) the anterior pituitary-like (luteinizing) hormone prepared from human pregnancy urine—Ant-S (206 days)
   (c) the urine extract prepared from normal (nonpregnant) female urine (172 days) and
   (d) the anterior-pituitary follicle-stimulating hormone prepared from pregnant mare's serum—Gonadogen (109 days);

2. The preparations that resulted in a high percentage of animals living longer than the maximum survival time of the control animals (longer than 135 days) are:

   (a) the anterior-pituitary follicle-stimulating hormone from pregnant mare's serum (41 per cent)
   (b) the urine extract prepared from normal (nonpregnant) woman (36 per cent)

(c) the urine extract prepared from normal men (32 per cent)
(d) the anterior-pituitary-like (luteinizing) hormone of human pregnancy urine (29 per cent)
(e) enterogastrone (orally), 21 per cent.

3. The preparations that resulted in a significant number of animals dying without ulcer are:

(a) the anterior-pituitary-like (luteinizing) hormone of human pregnancy urine (45 per cent)
(b) progesterone (33 per cent)
(c) the anterior-pituitary follicle-stimulating hormone from pregnant mare's serum (33 per cent)
(d) the urine extract from normal men (24 per cent) and the urine extract from normal (nonpregnant) women (21 per cent)

The percentage of deaths without ulcer was as high or higher in other series, but the results in the latter groups were not considered significant because the average survival time was lower than that of the control series; the percentage of animals that lived longer than 135 days was extremely low or zero, and most of the animals that died without ulcer died within 30 days of the Mann-Williamson operation. These apply to the series treated with the posterior pituitary extract plus A.P.L. hormone, orally administered A.P.L. hormone, parenterally administered enterogastrone, and inactivated A.P.L. hormone.

4. Epithelization of the ulcers was noted in a significant number of the animals treated with:

(a) progesterone (80 per cent)
(b) the anterior-pituitary-like hormone of human pregnancy urine (38 per cent)
(c) the heat inactivated A.P.L. hormone (38 per cent)
(d) oral (crude) A.P.L. hormone (38 per cent)
(e) the urine extract of normal (nonpregnant) women (31 per cent)

It is of interest to note that only 8 per cent of the ulcers in the series treated with normal male urine extract showed epithelization, similar in per cent of epithelization to that of the untreated animals. It is also important to stress that the per cent of epithelization in another series of Mann-Williamson animals treated with a urine extract prepared from ulcer patients (not included in this report) is also 8 per cent.[8] In other words, the per cent of epithelization is exactly the same (that is, 8 per cent) for each of the following three series of animals: the untreated series, the series treated with a urine extract prepared from normal men, and the series treated with a urine extract prepared from ulcer patients. The per cent of epithelization is significantly higher in the series of animals treated with extracts prepared from the urine of pregnant and normal (nonpregnant) women.

In this communication, "per cent ulcers with microscopic healing" (Chart I, item 4) includes *only* those ulcers which showed epithelization at the edges of the ulcers. However, some of the ulcers which failed to show

epithelization showed evidence of healing as noted by fibroblastic proliferation and proliferation of the capillaries. These are discussed more fully elsewhere.[12]

Chart I analyzes results of treatment on the basis of the four criteria just enumerated. It is evident, however, that an animal that has lived longer than 135 days might have died without an ulcer. Benefit of therapy is thus recorded in each of these two criteria. Similarly, an animal that has lived longer than 135 days might have died with an ulcer and the ulcer might have shown epithelization when it was examined microscopically. Here again the beneficial effect is recorded in each of these two criteria. If we attempt to correlate these four criteria into one (to exclude these apparent duplications) and at the same time take into consideration that death without ulcer, if the animal died within 30 days, is of no great significance, we note that best results were obtained in the series of animals treated with the following:

1. The anterior-pituitary-like (luteinizing) hormone of human pregnancy urine (Ant-S)*
2. The extract prepared from urine of normal (nonpregnant) women*
3. The anterior-pituitary follicle-stimulating hormone of pregnant mare's serum (Gonadogen)
4. Progesterone (Proluton)
5. The extract from urine of normal men*

The name Anthelone (Greek: anti, against and helkos, ulcer) was given to the anti-ulcer factor in urine which has a beneficial effect against the Mann-Williamson ulcers.[13]

DISCUSSION AND SUMMARY

Our studies have attempted to determine the effect on experimental Mann-Williamson ulcers of certain major hormones which are concerned in the reproductive cycle. It is well known that the hormones of the anterior-pituitary activate the gonads and the gonads, in response to this stimulation, elaborate their own internal secretions. These internal secretions (that is, androgens and estrogens) are all excreted in the urine of men and women, in pregnancy and in nonpregnant states, though in varying degrees. The anterior-pituitary principles (luteinizing and follicle-stimulating), the corpus luteum hormone (progesterone) and the urine extracts from normal women and men (Anthelone) appeared to be of greatest value in the healing of the experimental Mann-Williamson ulcers. Estrogens were without benefit.

The study is admittedly not complete, and the results not definitely conclusive. Our findings with the anterior-pituitary-like or luteinizing hormone of human pregnancy urine were corroborated by Broad and Berman.[14] We are of the opinion that our results to date warrant further study of the relationship of hormones to peptic ulcer.

*These three urinary extracts (pregnancy, nonpregnancy, and male) which we found effective against Mann-Williamson dogs were each assayed on hypophysectomized rats for adrenocorticotropic activity by means of the ascorbic acid depletion technique (courtesy Dr. Joseph D. Fisher, Armour Laboratories, Chicago, Ill.). These extracts had been prepared during 1940 (nearly nine years ago) and two of these (normal female and normal male) were kept in solution (dissolved in distilled water with 0.5 per cent phenol) in a standard office refrigerator during the nine years. The results obtained indicate approximately 1 per cent of adrenocorticotropic activity according to the Armour Standard LaIA, that is 1 mg. of each urinary extract contained from 10 to 15 gammas of ACTH, Armour Standard LaIA.

Neurohumoral and psychosomatic factors are now generally considered to play an important role in human peptic ulcer. If these factors are associated with the genesis and recurrence of peptic ulcer it is certainly possible that they may operate directly or indirectly through the endocrine glands. Correlated studies of this possibility are desirable.

ADDENDUM

The recent work of Hench[15] indicating the relationship between the pituitary-adrenal complex and rheumatoid arthritis, with clinical improvement following treatment with Compound E, is based on the often observed beneficial effects of pregnancy on this condition.[16] This observation parallels our own investigations on the protective effect of pregnancy upon peptic ulcer as summarized in 1938[3] and since augmented by numerous experimental and clinical studies. One of us (D. J. S.) thus raised the question whether the beneficial effect of pregnancy on human peptic ulcer might also be due to a pituitary-adrenal mechanism.[17]

It is well known that the pituitary is more active during pregnancy and possibly during the active sex life of the female. The pituitary adrenocorticotropic hormone (ACTH) stimulates the adrenal cortex to secrete its steroids. One of these adrenal cortical steroids, Compound E (17-hydroxy-11-dehydrocorticosterone), may have a beneficial and protective effect on peptic ulcer in the human being, just as it has on rheumatoid arthritis, and may well be the factor through which both these conditions are benefited by pregnancy.

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OSTEOPLASTIC MOBILIZATION OF THE ILIUM

A New Operative Approach to the Interior of the True Pelvis

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SURGICAL access to bony lesions situated in the interior of the pelvis has always presented serious difficulties from a technical point of view. In our present paper we propose to exclude from the discussion partial resections of the various parts of the pelvic skeleton, for the removal of localized bone lesions, such as tumors or tuberculous foci.

Our aim has been to develop an operative procedure which would give satisfactory access to the pelvic cavity with minimum trauma to vital structures, good drainage, and early functional repair.

The well-known incisions sponsored by Bardenheuer, Ollier, Rieder, Tillmanns, Kocher, Roux and, last but not least, by Sprengel, give surgical access in varying degree to the outer surface of the pelvis. Sprengel's incision, following the iliac creat, does to a certain extent allow approach to the iliac fossa and the medial aspect of the hip joint, but to attain this end the attachments of the abdominal muscles and the muscle insertions at the anterior superior iliac spine must be severed, with all attendant disadvantages. The protruding ilium furthermore presents a serious obstacle to successful management of deep-seated bony lesions. Working with the chisel or the burr is difficult and cumbersome, especially posteriorly and below the pelvic brim.

Osteoplastic mobilization of a greater or lesser part of the ilium, comprising the major part of the iliac crest and the anterior superior spine, leaving the attached muscles intact, seemed a logical way of solving the difficulties presented. The access gained is direct and ample, no vital structures are injured, drainage is good, and functional repair rapid. The operation is applicable to all localized extraperitoneal and bony lesions below the pelvic brim, such as bone abscesses, tuberculosis, foreign bodies, and fistulas involving bone. Although the operation would at first sight seem to be a formidable procedure, experience has shown that it is well tolerated and causes comparatively little shock. It is evident that patients should be conscientiously selected and prepared for the operation. An exact anatomic diagnosis should be sought by all available methods, such as stereoscopic roentgenograms, radiopaque fillings of fistulas, etc.

The operative procedure is best illustrated by Figs. 1 to 3. With the patient lying on his sound side and the operator facing him, a curved incision is carried right down to the bone along and slightly below the iliac crest. The anterior end of the incision can be continued past the anterior superior iliac spine down the thigh for about two inches, as this will facilitate mobilization of the bone (Fig. 1). The outer aspect of the ilium is then stripped of the gluteal

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muscles subperiosteally, to the edge of the great sciatic foramen. The large skin-muscle flap thus formed is retracted downward, so that the superior gluteal vessels are exposed (Fig. 2).

The part of the bone mobilized is marked with an *x* in Figs. 2 and 3. Careful experimentation on the cadaver has shown that this should always include the anterior superior iliac spine with the attached sartorius and tensor fasciae muscles. A narrow bridge of bone should be left at the great sciatic foramen in order not to break the continuity of the pelvic girdle. Posteriorly it is well to keep clear of the sacroiliac joint and its immediate neighborhood. The cancellous bone in this region is quite thick and the inner periosteum is reinforced by the anterior ligaments of the sacroiliac joint; hence, it will be found difficult to mobilize the bone sufficiently if the incision has been carried too far backward. The optimum line for chiseling will be seen in Figs. 2, 3, and 4. Sharp broad chisels of the Lexer type, or a circular saw can be used for cutting the bone.

Fig. 1.—Outline of the skin incision for osteoplastic mobilization of the hipbone.

The separated piece with its muscle attachments is pushed medially toward the lower abdominal cavity with considerable force. Subperiosteal stripping of the bone is continued downward on the inside toward the pelvic brim, and beyond when necessary. Occasionally (as in Case 3) it may prove more advantageous to displace the mobilized bone upward and outward for better access. A satisfactory approach is thus gained to the anterior aspect of the sacroiliac joint, the medial side of the hip joint, the descending part of the ischium, and the horizontal ramus of the pubis. The depth of the wound is crossed by the posterior femoral cutaneous nerve and by the common iliac vessels (Fig. 3).

Fig. 2.—The outer aspect of the hipbone is exposed subperiosteally and the muscle flap reflected downward, *e*, superior gluteal vessels; *f*, gluteal muscles reflected; *x* part of the hipbone mobilized.

Fig. 3.—The mobilized part of the hipbone (marked *x*) is displaced medially, exposing the inferior of the true pelvis. *a*, Iliac muscle; *b*, posterior femoral cutaneous nerve; *c*, common iliac vein; *d*, brim of the true pelvis; *e*, superior gluteal vessels; *f*, gluteal muscles reflected.

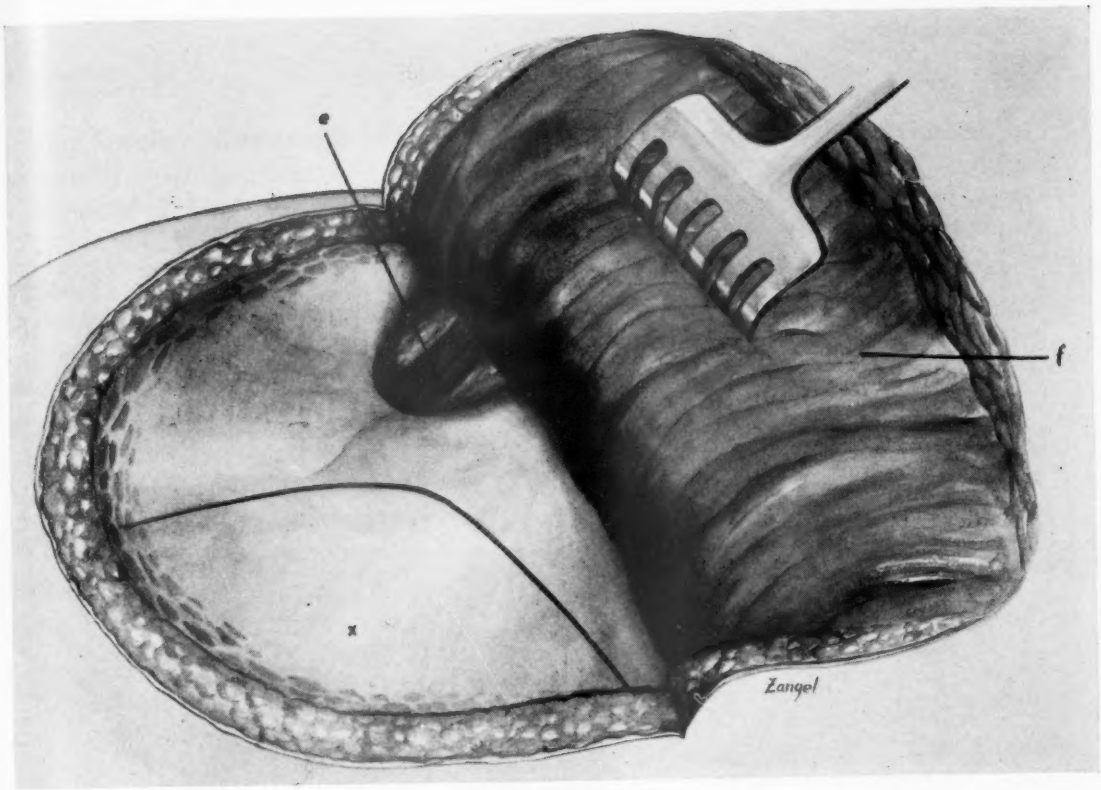

Fig. 2. *(For legend see opposite page.)*

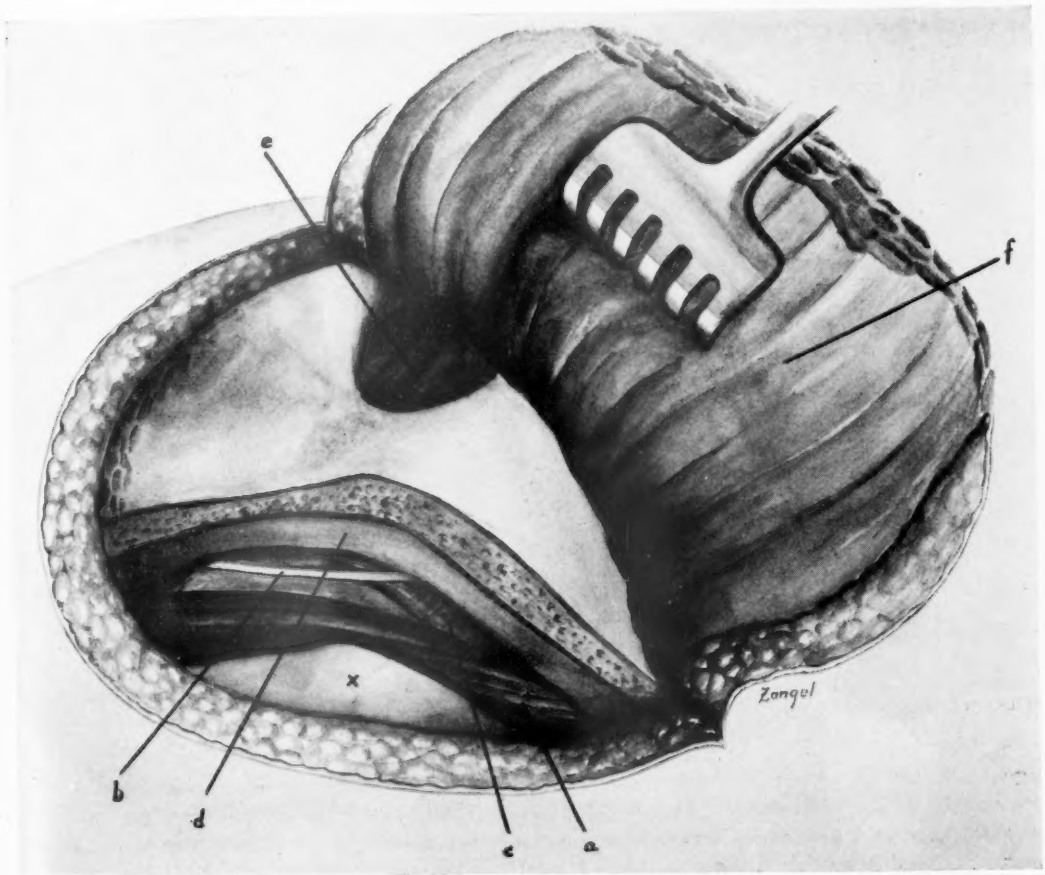

Fig. 3. *(For legend see opposite page.)*

At the end of the operation the mobilized part of the bone is replaced and the gluteal muscles are sutured to the iliac crest. Any remaining displacement has proved quite unimportant from a functional point of view, and no attempt need be made to attain perfect alignment by the use of wire sutures. Consolidation will be found sufficient within four weeks and no instability of the hip joint, due to muscular insufficiency, has been observed in any case.

Perhaps a few words should be said about the question of drainage. In two of our cases we have been forced to reopen part of the incision to drain an intrapelvic abscess through a trephine hole in the hipbone. This experience leads us to advocate immediate drainage through a suitably placed bone opening whenever findings at operation seem to make this desirable (Fig. 4). Four patients have so far been operated upon with very gratifying results.

Fig. 4 (Case 3).—Tracing from roentgenogram after osteoplastic mobilization of the hipbone for removal of a piece of shrapnel. Mobilized part of bone held in place by Kirschner wire. The central hole in the bone was made for drainage.

CASE 1.—A 19-year-old soldier had suffered from sciatic pains in the left hip since the age of 15. Movements of the hip joint were limited by pain. The x-ray examination showed narrowing of the joint space and cystic destructive foci in the acetabulum and the descending ischial ramus. All other findings being normal, a diagnosis of localized cystic bone disease was made and operation was performed by means of osteoplastic mobilization of the hipbone.

The bone foci were found to be caused by tuberculous abscesses. Healing took place smoothly but the later course led to ankylosis of the diseased hip joint.

CASE 2.—A 21-year-old man had been operated upon one year previously in another hospital. A history could not be obtained, but apparently an opening had been made in the ilium for drainage. The postoperative course had been stormy. When seen by us, the patient presented a fistulous opening near the anterior superior iliac spine on the right side. Radiopaque filling revealed a fistulous track entering the pelvic cavity through a hole in the ilium near the anterior part of the spine, and extending backward to the hollow of the sacrum and the great sciatic foramen.

At operation access was gained through osteoplastic mobilization of the hipbone, and the fistula was excised radically by cutting the sacrotuberous ligament. Three months later part of the incision had to be reopened to remove several small sequestra. After this, healing was rapid with complete functional recovery.

CASE 3.—A 30-year-old man in 1945 had received a shrapnel injury in the right lumbar region, just below the twelfth rib posteriorly. Several abscesses led to a permanent fistula

Fig. 5 (Case 4).—Tracing from roentgenogram (preoperative), showing radiopaque filling of fistulous track originating from gunshot injury of right wing of sacrum and of sacroiliac joint.

at the point of entrance. Roentgenogram showed a metallic foreign body 12 by 8 mm. just anterior to the right sacroiliac joint. A radiopaque filling of the fistula led from the external opening below the twelfth rib straight down to this foreign body. At operation the ilium was mobilized as described previously, but the mobilized bone was displaced upward and out instead of being pushed medially into the pelvic cavity. The foreign body was found in the scarred iliacus muscle and removed without difficulty. Drainage was instituted through the external fistula and the bone replaced and held by means of a Kirschner wire. Primary healing took place (Fig. 4) and the patient was discharged well fifty-one days after the operation.

CASE 4.—A 33-year-old man was wounded by a submachine gun in 1944, the point of entrance being at the left side of the sacrum. He had been operated on several times and the projectile removed. Unfortunately, a case history could not be obtained, owing to war conditions.

When seen by us in January, 1948, the patient complained of a continuous discharge from the right buttock. X-ray examination after filling with iodized oil showed a fistula traversing the buttock, entering the pelvic cavity just above the great sciatic foramen, and ending in a round bone defect in the sacrum near the sacroiliac joint (Fig. 5).

Surgical approach was by mobilization of the ilium: The fistula was entirely excised. The round bone defect was converted into a flat groove and through-and-through drainage was instituted. The bone was replaced and the gluteal muscles sutured into place. The postoperative course was complicated by an intrapelvic abscess and a mild osteitis of the wing of the ilium. Drainage was instituted through a large trephine hole and the infection cleared up promptly. After fifty days the patient was up and about, and at the time of writing (three months after operation) is practically well.

SUMMARY

A method of surgical approach to the interior of the pelvic cavity is described, making use of osteoplastic mobilization of the wing of the ilium. The method gives good access to this difficult field, with minimum trauma and no lasting functional impairment. The method is applicable to the treatment of lesions situated at the inner side of any part of the pelvic ring. Four patients thus treated are briefly reported upon.

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TRIGGER FINGER PRODUCED BY EXCESSIVE HEAT

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THREE cases of trigger finger are to be described, in all of which heat appeared to be the causative factor. Two of the three cases developed by using the same overheated arc welding gun for several months; the third followed exposure to Sollux lamp radiation for five minutes. They are of interest from the standpoint of pathology in general and of industrial and preventive medicine in particular. They gain in significance since in a recent Memorandum (1945) by the Factory Department of the Ministry of Labour and National Service the occurrence of trigger finger amongst arc welders was confirmed. "These were characterised by a locking effect when the fingers were fully flexed, and passive assistance was required to obtain full extension which was accompanied by a slight clicking sound." To my knowledge no trigger finger produced by and attributed to heat action has been recorded in the literature.

The trigger finger is a clinical and not a pathologic entity. It is the manifestation of a disproportion between tendon and tendon sheath, caused by a stricture of the sheath or by a thickening of the tendon or by both these changes simultaneously. Our knowledge of the etiology of the trigger finger is hazy; so much, however, seems certain that several different causes may lead to the same pathologic result. It is also probable that, in some cases, the coincidence of at least two factors is necessary for the development of the disease: one being the disposition, the other the exposition (trauma, etc.). The disposition is either local or general. The tendon sheaths of the digital flexor tendons have a natural anatomic stricture opposite the base of the first phalanx. This point is, therefore, most disposed to further constriction. The general disposition or constitution is more difficult to define. Perhaps the "arthritic" types of the French are more likely to be affected if exposed to certain irritations. One type of the constitutional trigger finger is more distinct, it is the congenital type (Konetschke, 1888; Berger, 1875). Cramer and Schleicher described trigger fingers in two uniovular twins.

The commoner form of trigger finger, however, is the acquired one, especially that of traumatic origin (Poulson, Tilmann). Rheumatism and gout are two other causative factors mentioned by several authors (Marchesi, 1905, etc.). Necker who collected 121 cases from the literature, found that 52 were of rheumatic or gouty origin, 13 of traumatic, 2 congenital, 47 due to occupational strain, and 7 of unknown etiology. Necker rejected the trigger finger as an industrial disease. Hauck thought that trigger finger was produced by trauma but he always postulated a special disposition because, in his experience, the disease was found chiefly in elderly women with arthritic complaints.

Kroh found signs of chronic inflammation of the tendon sheaths in 13 cases on histologic examination. But, in his opinion, these signs could not be attributed with certainty to an acute or chronic trauma. He does not regard any

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of his cases as being caused by occupational injury. In this respect he follows the great majority of authors who are just as unconvincing as Bertelsmann (1937), who records a self observation. In his surgical work he frequently used bone forceps and eventually developed a right trigger thumb. After an injury of the right arm he used the left hand preferably for bone work and developed consequently a left trigger thumb. Both disappeared after rest. Years later he strained the two small fingers by using a hoe for garden work and developed trigger finger in the two small fingers. In my opinion no more convincing example of an occupational trigger finger could have been adduced.

Rothenberg (1936) refused industrial compensation for a traumatic trigger finger with similarly unconvincing arguments. Only a few of the older authors recognized the occupational factor as being of primary importance: Schulte and Sudeck (1900) described fifteen cases of trigger finger caused by rifle butts, in young soldiers. Antegliano (1886) saw four cases of trigger finger of the right middle finger, produced by fencing. Its occurrence in pianists, seamstresses, and flutists is also known.

From this short review of the literature it is evident that the trigger finger is not recognized by the majority of authors as an industrial disease, and compensation is refused to those affected by it. It is the purpose of this paper to show that, in at least some cases, this view is untenable.

CASE REPORTS

CASE 1.—A man aged 33 years had measles, scarlet fever, and bronchitis as a child and had been healthy since. Syphilis, gonorrhea, and rheumatism were denied. From 1931 to 1935 he worked as an arc-welder. From 1935 to 1941 he did clerical work. He took up arc welding again in August, 1942. In September, 1942, his arc-welding gun became overheated so that his thumb blistered in spite of the asbestos gloves he was wearing for the work. He used this faulty instrument for six months, six to eleven hours a day. Work had to be interrupted after one-half hour to let the tool cool down. (The handle of a normal arc-welding gun is covered with rubber and its temperature is not felt through asbestos gloves.)

After having used the faulty tool for six months he noticed in the morning a stiffness of the right hand when he started using it. He changed his job and gun because he could no longer grip a hammer firmly. In November, 1942, the right middle finger started jerking; the same condition developed three months later in the right ring finger. Soon both fingers locked and could not be opened without effort.

On examination, on Dec. 18, 1942, he presented signs of definite trigger finger of the middle and ring fingers; their extension was difficult and was accompanied by an audible click and a visible jerk. Nothing abnormal could be palpated. He was treated for three months with radiant heat and massage but did not improve.

At operation* on March 4, 1942, both flexor tendon sheaths were exposed 4 cm. proximal and 4 cm. distal from the metacarpophalangeal joints. They were found thickened and narrowed; they were slit and partially excised. No pathologic changes of the tendons were seen.

The clicking disappeared after operation, but the patient was unable to close the two fingers fully. He went back to arc welding in March, 1943, and this time used a normal gun. He has never regained full power in the two fingers operated upon. In May, 1943, the middle finger started locking again and the patient was unable to open it without the help of the other hand.

*By A. M. A. Moore.

At the second operation,* July, 1943, adhesions and regenerated parts of the two tendon sheaths were excised. This operation did not improve the fingers. In September, 1943, the extension of both fingers became restricted and the clicking of the middle finger recurred. Since then the condition remained stationary; galvanization and diathermy had no beneficial effect.

On examination, December, 1943, the operation scar of three inches over the middle finger was adherent to the flexor tendon, that over the ring finger was mobile and smooth. The active extension of both fingers in the metacarpophalangeal joints was reduced by 15 degrees; extension in the other two joints was full. The active flexion of the two end and middle phalanges was reduced by 30 per cent. Passive flexion was possible only against considerable resistance. During flexion of the middle finger a click was audible which could be eliminated by pressing on the flexor tendon over the basal phalanx. The three other fingers were normal. The grip was poor.

December, 1946, the last operation did not improve function. Both fingers were held in semiflexion and could not be extended actively to full extent. The click in both proximal interphalangeal joints was still present. There were vasomotor changes in both fingers.

CASE 2.—A man aged 33 years, came from a healthy family. He was operated upon for a lung abscess twelve years before admission; he had no complaints afterward. He had no syphilis, no gonorrhea, no rheumatism. From the age of 16 to 20 years he worked as a stationary packer; from 20 to 30 years he did no manual work. From April, 1941, to August, 1942, he did arc welding for ten hours a day. From October, 1942, he *used for four months the same faulty tool as the man described as Case 1.* Though he packed the gun handle with a rag the heat penetrated his asbestos gloves and the tool felt uncomfortably hot. He never actually burned his hand. From January, 1943, he used another gun.

In March, 1943, he felt pain across the right palm during strenuous work. In May, 1943, the right ring and small fingers started locking every morning. Rest improved this condition for six weeks. In June he had a recurrence for a short period; since August, 1943, the complaints became constant.

On examination, Sept. 21, 1943, the configuration of the right hand and fingers was normal except for the ring and small fingers being pressed firmly into the palm. The active extension of the two fingers and the middle finger was impossible, the passive extension very painful. After their forced extension function improved, but active extension of the small finger was still reduced by 50 per cent and accompanied by a click. There was no muscular atrophy; all movements of the other two fingers and wrist were normal.

At operation in October, 1943, incision was made of 6 cm. over the flexor tendons in the region of the first phalanx and head of the metacarpal bones of the third, fourth, and fifth fingers. The three tendon sheaths which appeared thickened and constricted were slit and partially excised in the exposed area. The tendons were normal in appearance and moved freely after liberation. There was a normal course of healing.

In November, 1944, the patient had no power in his three fingers and was unable to bend them.

In February, 1944, light pentothal anesthesia was given. The patient responded to commands but was unable to bend the three fingers. Manipulation under deeper anesthesia showed adhesions in the incision areas. After this manipulation the finger movements improved slightly. The patient did not reappear for re-examination.

CASE 3.—This was a man aged 80 years. At the age of 15 years he had suffered from tuberculous coxitis with subsequent subluxation. Eleven years before admission he had had a right hemiplegia from which he recovered completely. He limps and uses a stick for walking. He had no syphilis, no rheumatism, no gonorrhea.

Two and one-half years previously, when he had *infrared treatment (Sollux lamp)* for arthritis of the left knee, this became so hot that he had to cover it for protection with the

*Also by Moore.

left hand *for about five minutes.* The hand became extremely hot but was not actually burned. Four to five hours after this treatment he felt a stiffness in the left middle finger and could not extend it without effort. Movement was accompanied by a click. A similar condition of the ring finger developed one week later. Both fingers were treated with Sollux lamp for five weeks. They did not improve and remained unchanged afterward.

On examination the man was found to be in relatively good general condition. The right hip was subluxated on account of an old tuberculous coxitis. There were no signs of any active tuberculous process or hemiplegia. The configuration of the left hand and fingers was normal. Nothing abnormal was palpable. The active flexion of all fingers was full and free. The extension of the middle and ring fingers in the metacarpophalangeal joints was also full, but in the first interphalangeal joints it was reduced by 50 per cent. This restriction could be corrected only with great effort against strong resistance, with the help of the other hand; it was accompanied by a jerk and click. Extension in the other joints is full.

COMMENT

The three cases described are all typical cases of trigger finger. All three developed after exposure to excessive heat. While in Cases 1 and 2 there was exposure to high temperature over a longer period of six and four months, respectively, in Case 3 exposure was only for five minutes. In all three cases the localization of injury was restricted to the area exposed to heat, and in all three there was a continuity between trauma and injury. In Cases 1 and 2 the same overheated tool was used under similar circumstances, for the same purpose, for about the same length of time, with the same pathologic result.

In the first two cases no sign of any constitutional disposition could be detected; both were healthy, young men, with no history of previous arthritis or local injury. One patient (Case 3) had previously arthritic complaints in his knee, but they were due to static conditions in consequence of a tuberculous hip. This patient was a very intelligent and critical man; he was very definite about having had no trouble with his hand previous to its exposure to Sollux lamp radiation and insisted that the complaints started on the day of overheating. This was testified by a witness, a reliable masseur of the hospital who knew the man years before and after the heat incident. A compensation claim did not arise.

Our three cases were observed two years before publication of the Ministry of Labour's *Memorandum on Electric Arc Welding* which described the occurrence of trigger finger amongst arc welders (no figures were mentioned). This Memorandum confirms my opinion that the trigger fingers of the first two patients (Cases 1 and 2) were the direct result of using an arc-welding gun, and that trigger finger in arc welders thus is an industrial disease. The Memorandum expresses the tentative view that the very frequently repeated gripping effort—perhaps 200 to 300 times a day, required to release the spent electrode and insert a fresh one—seems to be the precipitating cause of the trigger finger.

While it is difficult to refute this view, the fact that in my two cases trigger finger developed in two men who used the same faulty tool, which differed from other tools only in so far as it became unduly hot, makes it more than probable that, in some cases at least, it is the heat and not the repeated gripping effort which is responsible for this disease. It would be of interest to investigate in the future whether those workers in the arc welding industry who develop

trigger finger used a gun which became hotter than other guns or whether, perhaps, these workers were less protected against heat by suitable gloves than those workers whose hands were spared from injury.

If my explanation proves to be correct it will be necessary to watch for trigger fingers in other branches of industry in which overheating occurs. It will be necessary to take more precautions against overheating of tools in general. It will be necessary to watch also whether the different forms of heat treatment, like diathermy, short-wave diathermy, infrared, produce trigger finger when applied over a longer period.

Heat may also prove to be an adequate trauma to produce trigger finger experimentally in animals and thus facilitate the study of this disease, so little understood.

The three cases reported are of interest also because they seem to show that trigger finger can develop in healthy individuals, irrespective of constitution, provided an adequate trauma is applied. It is very unlikely that two healthy young men using the same hot tool should develop the same pathologic condition with the same localization, within practically the same period, because of a similar faulty constitution, and not because of the identity of trauma.

The constitutional factor can, naturally, never be completely excluded from playing a part in the development of any pathologic condition. Even when a man is killed by a brick falling upon his head his constitution is a contributary factor to his death, still one would attribute the death to the trauma. It is the quantitative estimation of the two factors, constitution and exposition, which determines whether a disease is considered constitutional or not. As mentioned earlier, compensation was refused by other authors to industrial workers who developed trigger finger during their work because their constitution was made more responsible for their injury than their exposure to trauma. It is from the standpoint of the worker's compensation that the question of constitution in relation to trigger finger is not only of academic but also of practical importance.

I consider that in every case of trigger finger in which continuity between a chronic or acute trauma sustained during work (pressure on tendons, frequent movements, heat) can be proved, without evidence of previous localized pathologic changes, the worker's right to compensation should be recognized. My observation suggests that in at least some cases trauma is by far the more important factor in producing trigger finger, as far as heat is concerned, and there is nothing to prove the contrary with regard to other traumas.

I recently saw two further cases which confirm me in this conviction: One concerned a Land-Army girl 20 years of age who did no manual work in civilian life. After using a trowel for planting for several days she developed a typical trigger thumb. The other was a woman 40 years of age who spent over twenty years cutting carpets with large scissors. She also developed a trigger thumb of the right hand. In neither case was there any tangible sign of a constitutional disposition. I considered both cases to be occupational injuries entitled to compensation.

It was suggested by Kroh that there is a similarity between trigger finger and de Quervain's tendovaginitis stenosans. He saw a difference between the two in the fact that while in the latter a chronic repeated trauma is always the causative factor, this is not so in the case of the trigger finger. My observations make the suggested difference between the two syndromes very unlikely. The two are most probably identical clinical entities.

Only two of these cases were treated surgically. As seen, the results of both were very unsatisfactory, in great contrast to the excellent results obtained in other cases of trigger finger not produced by heat. A recent paper (Fogh-Anderson, 1947) shows that, out of 121 cases of the latter group treated surgically, 119 were cured by the first operation and the other 3 by the second operation. I cannot offer a satisfactory explanation for the bad prognosis of the first group. It is, however, possible that the tissue reaction to moderate heat is very protracted, and that the fibrosing process goes on long after the irritating factor, the heat, has ceased, similarly to an aniline or x-ray cancer which develops years after exposure. If this assumption were correct it might be necessary to operate on these patients in whom the condition was produced by heat at a later period than we did, when a further fibrosing process is no longer to be expected. Experience may, however, show that these patients should not be treated surgically at all. It may also be wrong to give them Sollux lamp and other heat radiation for treatment.

RÉSUMÉ

Three cases of trigger finger are described. There is circumstantial evidence that they were caused by excessive heat. Two patients handled the same overheated arc-welding gun, the third had an overdose of infrared radiation.

The recognition of the trigger finger as an industrial disease and the worker's right to compensation, under certain circumstances, is advocated.

Acknowledgment: I wish to thank Mr. A. M. A. Moore for allowing me to publish one of his cases, and Mr. Allan for re-examining one of the patients (Case 1) for me.

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RADIODERMATITIS AND NECROSIS

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"IT WOULD be rational to expect that with the advances made in the knowledge of the proper dosage of Roentgen rays, burns from this source would become less and less frequent. As a matter of fact, this does not seem to be the case, as in my own practice, I am seeing these burns even more frequently than five years ago when I presented a paper on the radical treatment of Roentgen ray burns, before the American Surgical Association."[1] These were the opening remarks by Dr. John Staige Davis at a meeting of the Southern Surgical Association in 1925. Now, twenty-three years later, we feel that much the same statement could be made.

All too often, the radiodermatitis or necrosis is the result of treatment of a chronic benign condition, especially dermatologic lesions, or is the result of negligence or ignorance. Further, we believe that the repeated use of radiation therapy in skin cancers, where radiation has failed previously, is a pernicious practice often resulting in an exquisitely painful, necrotic wound showing little tendency to heal. In addition, in those cases where the use of radium or x-ray therapy is optional or questionable some other form of treatment which does not have the dangerous potentials of radiation therapy is indicated.

The lesions under discussion have been classified into three groups by Porter.[2]

Group I.—Lesions resulting from a single massive dose, intentional or otherwise, or a few exposures at short intervals. For example, prolonged fluoroscopy, forgetting patient during treatment, or excessive dosage in treatment of malignancies. There are occasions when a history of exposure to radiation cannot be obtained from the patient. This is illustrated by one of our patients who had what was obviously a radiation ulcer. He was unable to give us any history of exposure. Inquiry of the patient's doctor revealed that repeated fluoroscopic examinations had been carried out for reduction of a fracture while the patient was anesthetized.

Another patient was referred with an exquisitely painful lesion of the back, which had resisted all therapeutic attacks for several months, including three "small x-ray treatments." Previous local applications had produced a black, adherent eschar, which obscured the true nature of the lesion. An early diagnosis of herpes zoster further confused the picture. However, at the time of surgical excision, the typical pathology of excessive radiation was noted. Detailed questioning finally brought out the history of fluoroscopy of the gastrointestinal tract preceding the onset.

Group II.—Patients receiving many exposures over a long period of time, in the treatment of various benign conditions such as acne, eczema, psoriasis,

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lupus, plantar warts, etc. Extreme caution on the part of the therapist in the treatment of these conditions is indicated. There is a strong temptation to renew the treatment when the lesion recurs and to minimize the latent effect of the previous radiation. Many times the patient is guilty of "shopping around," and unwittingly subjects himself to overtreatment. A very careful history should prevent this.

Group III.—Professional roentgenologists.

We have had occasion to see 25 patients in Group I, 16 in Group II, and 2 in Group III, for a total of 43 with radiodermatitis or necrosis (Table I).* Of the entire group, only 7 cases were justified. By that we mean that some other form of treatment would have given equal or better results without the sequelae of excessive irradiation. There were 14 cases of skin cancer in which repeated radiation therapy resulted in necrosis of soft and/or bony tissues; some form of surgery would have been better. There were 14 benign or dermatologic conditions, including 6 patients with plantar warts. Prolonged fluoroscopy was the cause in 3 patients.

In the way of prevention, the greatest progress has been made in reducing the number of victims in Group III. Present-day roentgenologists are well aware of the damage that occurs from frequent exposure and take proper precautions. A big factor in the production of radiodermatitis is the latent period, together with the fact that repeated doses have a cumulative effect. The radiotherapist is often unaware of having produced a burn because it may not become evident for months or years, or the patient may not return.

TABLE I

	NUMBER OF CASES	
	JUSTIFIED	UNJUSTIFIED
Benign conditions		15
Malignant	7	
Malignant, but other forms of treatment better		19
Total*	7	34

*Two cases in Group III not included in this table.

Pathology.—Radiation, whether from x-ray or radium, is destructive to living tissue. Wolback[3b] and others[4] have described the pathologic findings of excessive irradiation. Briefly, the pathology in chronic radiodermatitis consists of hypertrophy of the epithelium, atrophy of the corium, with loss of the sebaceous glands, hair follicles, and sweat glands, in that order. There is a marked obliterative endarteritis affecting all vessels, and seriously reducing the blood supply to the area (Fig. 1).

Grossly, an area of chronic radiodermatitis has a very typical appearance which is not easily confused with any other condition. The skin has an

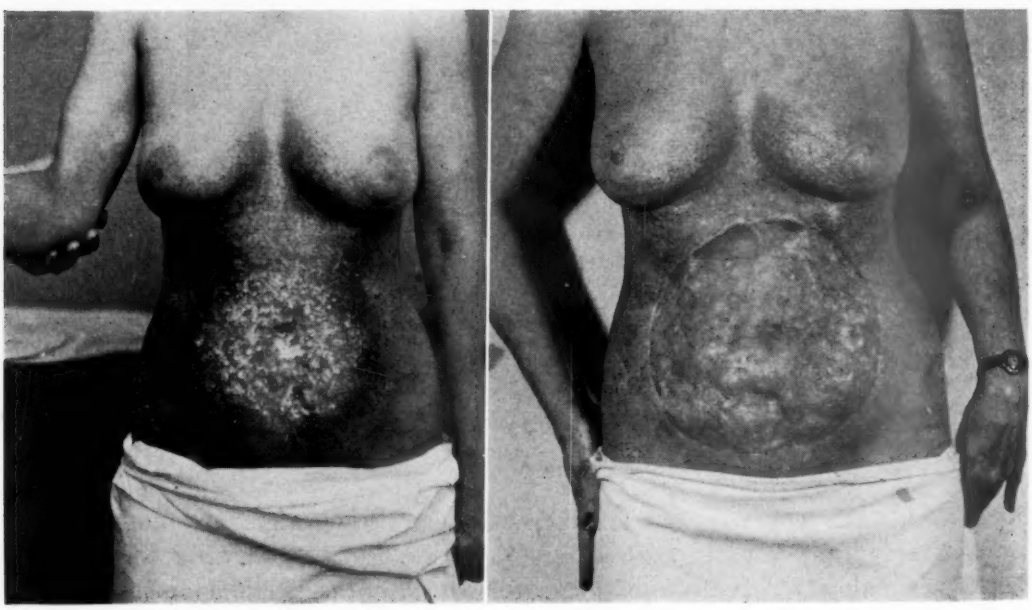
*Since this paper was submitted for publication, 11 additional patients have been seen, 5 in Group I, 5 in Group II, and 1 in Group III. Four of the cases resulted from the treatment of benign conditions, while 6 resulted from the treatment of malignant disease, but other forms of treatment would have been better, therefore, all 10 of these would be classified as unjustified. The patient in Group III was a dentist who received his burn from holding the film in the patient's mouth.

atrophic, tight appearance which is particularly noticeable where the condition occurs over the face. The skin surface is dry, and many telangiectatic vessels can be seen. Keratoses are common, and small to large ulcerations may occur. These usually heal slowly, or, eventually, not at all. In more advanced cases where the radiation effect has been deep, all of the tissues may have been reduced to a firm, scarred mass, usually somewhat depressed below the surrounding surface and adherent to deeper structures. In such lesions, persistent, chronic, ulcerations are likely to occur. The surface of the

Fig. 1.—This patient received x-ray therapy for a cyst of the tibia. A cancellous bone graft was later required because of a fracture. The flap, which would have been entirely satisfactory with normal tissues, became gangrenous due to impairment of the circulation secondary to the x-ray therapy. The skin outwardly appeared to be normal.

ulcer is usually covered with a yellowish coagulum which may be easily removed, revealing a pale, yellowish, unhealthy base. Sloughing tissue separates very slowly, often requiring weeks or months. The blood supply of bone is easily damaged by irradiation and may succumb to the slightest infection. Characteristically, the dead bone is slow to sequestrate (Fig. 2). Daland[5] cited cases of bone remaining exposed and inert for five to seven years.

Fig. 2.—This patient, illustrative of Group II, received many radium applications in the treatment of a recurrent basal-cell carcinoma. The bone was exposed and inert over a period of four years. An important point to be noted is the futility of drilling holes in heavily irradiated bone for the purpose of producing granulations. Seven patients in this series developed bone necrosis.



A. *B.*

Fig. 3.—This patient had received radiation over a period of several years (Group II) for an obscure abdominal condition. She developed itching, burning, and pain, so that excision and skin graft were required. A split-skin graft was possible here because she had not received penetrating rays. *A*, Before; *B*, after.

Pain is an outstanding feature of all deep burns. It usually does not occur until late, except where massive doses have been given in one or several closely spaced treatments, in which case ulceration and severe pain may develop within a few days. Porter[3a] stated that the pain and agony of inflamed x-ray lesions is almost unequaled by any other disease. One of our patients was seen by the psychiatric service to evaluate the pain and the question of narcotic addiction. In chronic radiodermatitis, where the radiation has been received in multiple doses over a long period of time, itching, burning, and dryness of the skin are characteristic (Fig. 3).

Chronic radiodermatitis, once established, tends to get worse with the passage of time. In any event, the damaged tissue is a potential source of trouble, as it may become necrotic or undergo malignant degeneration at any time. Porter[2] and Davis[1] both noted that carcinoma was more likely to develop in those patients who had received small, repeated doses. This observation has been borne out in the four patients in our series who developed cancer in areas of radiodermatitis. Two were in Group II and two in Group III.

TREATMENT

In regard to the treatment in these cases, there is one outstanding fact that should be understood before any treatment is undertaken. Certain irreversible changes have occurred in the tissues, resulting in loss of healing and reparative powers, and for this reason, any treatment which does not involve removal of the diseased area, can be palliative in nature only. In our opinion, palliative treatment is of value in the following situations: (1) acute ulcerations, (2) for symptomatic relief of the early or mild radiodermatitis, (3) where surgery is refused or otherwise cannot be performed.

For the acute ulcerations, moist dressings of saline or boric solutions are helpful. Soothing ointments and lotions are also of value. Many authors speak highly of the value of fresh leaves of the *Aloe vera* plant.[6, 7] Most patients will require analgesics for relief of pain.

Radon ointment[8-11] has been tried by many writers since it was first introduced by Uhlmann[12] and, apparently, some improvement has been noted in certain cases. We have had no experience with the preparation, but a consideration of the destructive and irreversible changes that have taken place in the tissues would seem to offer little hope for real improvement in the process.

The surgical measures at our command may be listed as follows:

1. Electrodesiccation and coagulation
2. Excision
   (A) With closure
   (B) With skin grafting
   (C) With pedicle grafting
3. Amputation

The simplest surgical procedure is that of electrodesiccation or coagulation. This method is best indicated in the handling of keratotic lesions which are prone to occur in the cases of Groups II and III. It is particularly useful on the hands and face where the keratoses, or early epitheliomas, may be co-

A. *B.* *C.*

Fig. 4, *A*, *B*, and *C*.—This patient was given over 20,000 r x-ray therapy for a carcinoma of the cervix in 1940. She developed a radiodermatitis over both buttocks, as well as the areas shown here. The inguinal regions became extremely painful. Because of the destruction of the blood supply, pedicle tissue from the abdomen was required, as the areas would not support a split graft. The relief of pain and other characteristic symptoms was dramatic.

agulated as they appear. It is not advisable to coagulate large areas on the hand, since the resulting scar contracture may limit function.

Excision and closure are indicated whenever possible. Most cases of chronic radiodermatitis are too extensive for simple closure of the wound after excision, and it is here that split-skin grafts are indicated. These are suitable on almost any part of the body with the following exceptions: On the plantar surface of the foot, this graft is not satisfactory for weight-bearing, and on the palmar surface of the hand, it is subject to contracture. Likewise, it may contract when used on large areas on the cheeks, and the cosmetic result is poor.

Very large areas may be covered with split-skin grafts. As a rule, it is best to apply the graft immediately at the time of excision. There are, however, two situations in which a delay of three to ten days in grafting is indicated. If there is uncontrollable oozing from the wound, a graft would not be successful. Where there is a moderate amount of damage to the deeper structures, a better take of the graft may sometimes be obtained by permitting granulations to form. Delay in application of the graft may also reveal that the excision has not been radical enough because necrosis may take place in certain areas. A graft which had been placed over such an area would, of course, be lost.

The pedicle graft is indicated where there has been considerable damage to the deeper structures (Fig. 4). In such cases, the tissues are so avascular that a split skin graft would not take. Before surgery, one should attempt to evaluate the depth of the damage, so that the proper type of coverage can be planned. Knowledge of the amount and type of radiation that has been given is helpful. If the scar is hard, thick, depressed, and bound to the deeper structures, a pedicle flap will almost certainly be indicated. Ideally, all avascular tissue should be excised completely. In some instances, however, it will be found impossible to carry this out, as important structures, such as the great vessels, may be involved.

Amputation is indicated on the hand when an area of radiodermatitis has become malignant and invaded the deeper structures. It may also be necessary when infection occurs with destruction of tendons, etc.

SUMMARY

1. A plea is made for a greater recognition of the potential dangers of radiation therapy in both benign and malignant conditions.

2. Radiation therapy should be avoided in benign conditions wherever possible, particularly in those that are prone to recur or become chronic.

3. The persistent use of radiation therapy in skin cancers where it has failed initially is condemned.

4. Chronic radiodermatitis and necrosis are essentially surgical problems. Any measures short of extirpation can be palliative only.

5. Split-skin grafting is indicated where the damage is essentially superficial.

6. A pedicle graft carrying its own blood supply must be used where damage has involved deeper structures.

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THE LIGAMENT OF TREITZ AS A BARRIER TO INTESTINAL INTUBATION

A Clinical and Anatomic Study

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THE ligament of Treitz has not received the attention that it deserves as a barrier to intestinal intubation. Surgeons generally are interested only in whether or not the intestinal tube head has passed through the pylorus. From then on, the tube is supposed to pass down the gastrointestinal tract without any difficulty. Once the tube head is shown by radiography to be in the duodenum, then the intubation is considered as being successful. Unfortunately, in many cases the tube head passes through the pylorus with ease only to become arrested at the distal end of the third portion of the duodenum. It may remain at this location for days with the result that complete intestinal decompression is not obtained.

In studying this problem, two important factors were soon found to be responsible for this barrier to an otherwise successful intubation: on the one hand, the length of the ligament of Treitz, and on the other, the weight of the fluid and gas-filled loop of jejunum into which the duodenum empties.

That the ligament of Treitz played a very important role in intestinal intubation became increasingly apparent in a study of all patients intubated during the past five years. It should be quite obvious that an intestinal decompression tube whose downward progress was arrested at the duodenojejunal flexure would not be as effective a decompression unit as the tube would be in the ileum. For this reason, the importance of any barrier to an otherwise successful intubation must not be minimized.

Anatomists describe the ligament of Treitz as a suspensory muscle of the duodenum. It is described as a bundle of involuntary muscle fibers running from the left pillar of the diaphragm to the duodenojejunal angle.[1] Cunningham[2] described the ligament of Treitz as a muscular band that springs from the right crus of the diaphragm on both sides of the esophageal opening. It then descends over the left crus behind the celiac plexus, the splenic and left renal veins, and the pancreas, and then inserts into the duodenojejunal flexure. In children, this muscle is well marked and easily isolated and some of its fibers can be traced into the root of the mesentery where they are inserted into the peritoneum. In the adult, it becomes ligamentous and loose and is difficult to distinguish from the surrounding fibrous tissue.

The function of the ligament of Treitz is the support of the duodenojejunal flexure. It is thought to prevent this flexure from being dragged downward by the weight of the jejunum. In this fashion, it tends to keep the fourth portion of the duodenum at a relatively fixed point.

All anatomists have adequately described the marked variation in the curve of the duodenum as a result of the variation in the position of the third portion

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of the duodenum. The third portion of the duodenum is described as being either nearly horizontal and the fourth part as nearly vertical, or the third part may incline upward as it passes to the left and then it would lie in line with the fourth portion of the duodenum.

Because of the clinical observations relative to blockage to intubation at this point, it was decided to study anatomically the reason for this.

METHOD

The area of the duodenojejunal flexure was dissected out in thirty-five cadavers and the angle between the second, third, and fourth portions of the duodenum noted. In all cases, the length of the ligament of Treitz was determined by measuring from its point of attachment to the vertebral column as its upper point and the superior surface of the third portion of the duodenum to which it attaches as its lower point. No attempt was made to measure the length from the esophageal opening or from the left pillar of the diaphragm because that portion of the ligament of Treitz resting upon the vertebral column would constitute a fixed area and would not influence the angulation at the duodenojejunal flexure. It was noted that there was a considerable variation in the obliquity with which the third portion of the duodenum passed from right to left and that this variation in obliquity of the third portion of the duodenum was associated with a concomitant variation in the length of the free portion of the ligament of Treitz. By free portion of the ligament of Treitz is meant that portion of the ligament and its peritoneal fold distal to its attachment to the crura of the diaphragm and vertebral bodies.

Just as the position and type of the stomach seems to be associated with the body build or habitus of the individual, so also does the angulation of the third and fourth portions of the duodenum appear to vary with the length of the ligament of Treitz. In individuals with a short ligament of Treitz, the third portion of the duodenum was invariably found to angulate upward at an acute angle in its passage from the right to left. The shortness of the ligament of Treitz in this type of individual would result in a rather marked angulation at the duodenojejunal flexure. On the other hand, individuals with long ligaments of Treitz presented a third portion of the duodenum almost horizontal in its passage from right to left. In these people, the duodenojejunal angle was almost nonexistent since the fourth portion of the duodenum and jejunum lay on almost the same level.

In studying and reviewing the observations in Table I the angulation of the third portion of the duodenum has been classified into three main groups. These groups are: Group 1, all cases in which the third portion of the duodenum was found to take a horizontal course in its passage from right to left; Group 2, all cases in which the third portion of the duodenum was found to take an acute angulation in its passage from right to left; Group 3, all cases in which the third portion of the duodenum was found to angulate upward from right to left but whose angle was moderate in degree.

TABLE I. RESULTS

CADAVERS	LENGTH OF LIGAMENT OF TREITZ (IN INCHES)	DIRECTION OF THIRD PART OF DUODENUM
1	2	Horizontal
2	1	Oblique (moderate)
3	1	Oblique (moderate)
4	1	Oblique (moderate)
5	½	Oblique (acute)
6	½	Oblique (acute)
7	1¼	Oblique (moderate)
8	½	Oblique (acute)
9	½	Oblique (acute)
10	½	Oblique (acute)
11	1	Oblique (moderate)
12	1	Oblique (moderate)
13	1¼	Oblique (moderate)
14	1	Oblique (moderate)
15	½	Oblique (acute)
16	1	Oblique (moderate)
17	½	Oblique (acute)
18	½	Oblique (acute)
19	½	Oblique (acute)
20	2	Horizontal
21	2½	Horizontal
22	1	Oblique (moderate)
23	¾	Oblique (acute)
24	¾	Oblique (acute)
25	¾	Oblique (acute)
26	1½	Horizontal
27	¾	Oblique (acute)
28	2½	Horizontal
29	2½	Horizontal
30	1	Oblique (moderate)
31	¾	Oblique (acute)
32	1½	Horizontal
33	¾	Oblique (acute)
34	1	Oblique (moderate)
35	2	Horizontal

In Group 1, a horizontal direction was noted taken by the third portion of the duodenum in its passage from right to left. In these cases the duodenojejunal flexure was not acute. In fact, in many there did not appear to be any angle at all. All the cadavers in this group were found to have a ligament of Treitz that was fairly long. In all the cases that were dissected out it was found that in this group the ligament of Treitz ranged from one and one-half to two and one-half inches long. Whenever the ligament of Treitz was found to be two inches long or longer, the direction taken by the third portion of the duodenum was invariably horizontal in its passage from right to left. Fig. 1 is a good example of this group. Note that the angle between the duodenum and jejunum is not acute. Figs. 2 and 3 demonstrate clinical cases which could be classified in the same group. Note the direction taken by the intestinal tube in its passage through the third portion of the duodenum. Note also the downward drag of the mercury-containing balloon upon the tube in the jejunum. This type of case is the easiest to intubate and the least likely to impede the downward passage of the intestinal tube.

In Group 2 can be seen a well-marked angulation upward of the third portion of the duodenum associated with which there was a rather acute angle at

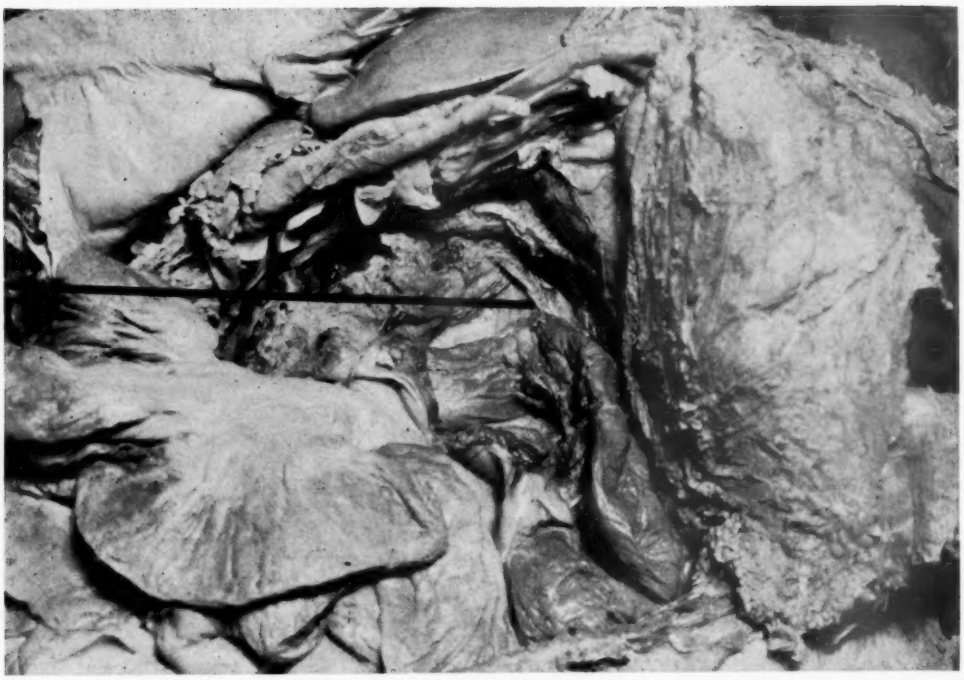

Fig. 1.—The horizontal position of the third portion of the duodenum. Angle at the duodenojejunal flexure not acute.

Fig. 2.

Fig. 3.

Fig. 2.—Note the absence of an angulation at the duodenojejunal flexure. There is a downward pull of mercury-containing balloon tip on intestinal tube.

Fig. 3.—Horizontal position of the third portion of the duodenum, with right angle at the duodenojejunal flexure.

the duodenojejunal flexure. In this group the ligament of Treitz was found to range from one-half to three-quarters inch in length. Fig. 4 is an example of this type of case. This cadaver presented a ligament of Treitz one-half inch long. Note the acute angle at which the third portion of the duodenum passed from right to left. In this case, the duodenojejunal angle was found to be very acute. It was straightened out in this figure for purposes of photography. Fig. 5 demonstrates a clinical example of this group. Note that in this figure the angle at which the third portion of the duodenum passes upward from right to left is so acute that a definite kink is made in the intestinal tube at the junction of the second and third portions of the duodenum. In using intestinal tubes of small luminal diameters such a kink might well occlude the tube at that point. In this patient the intestinal tube did not progress beyond this point for three

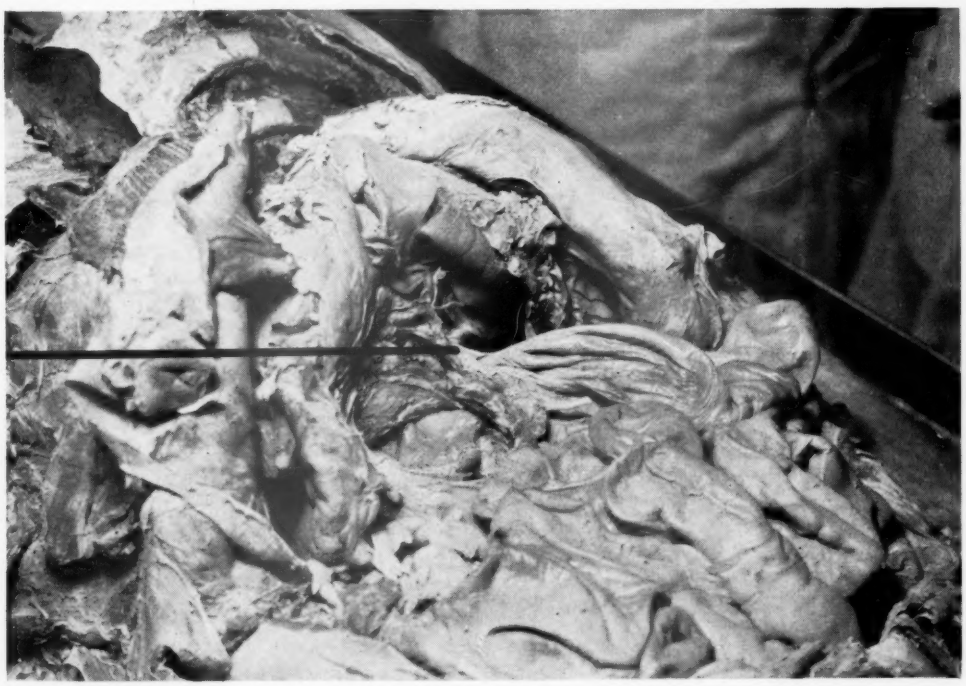

Fig. 4.—Note very acute upward angulation of the third portion of the duodenum. Ligament of Treitz very short—one-half inch.

days. When the patient was ambulatory it was soon noted that further downward progress of the tube was rapid. An examination of Fig. 5 suggests that the downward pull of the mercury-containing balloon at the tip of the tube was most efficiently utilized by ambulating the patient. Since making this observation it has been found necessary frequently to ambulate the patient in order to prevent arrest of the tube at the duodenojejunal flexure in this type of case. This was done without any hesitation even in the presence of an ileus due to peritonitis. In fact, most of the cases in which this arrest occurred were found as a result of peritonitis.

When it is considered that in such cases the intestinal distention is the result of fluid as well as gas within the bowel, and that the proximal jejunum so filled

is heavily weighted it becomes obvious that the downward drag of the weighted jejunum would markedly increase the obliquity of the duodenojejunal flexure. In some cases, the downward pull of the proximal jejunum is such that the duodenum is blocked at that point. This is especially likely to occur in paralytic ileus if a short ligament of Treitz results in an acutely angulating third portion of duodenum. Ambulation in such patients, after the tube head has dropped into the jejunum, is essential to further downward progress of the tube. Fifteen of the cadavers (43 per cent) were found to be in this group.

Fig. 5.—Acutely angulated third portion of the duodenum. There is a kink in the intestinal tube at the junction of the second and third portions of the duodenum.

Group 3 consisted of all those cases in which the third portion of the duodenum was found to angulate upward from right to left, but the angle was intermediary between Groups 1 and 2. In this group, the average length of the ligament of Treitz was found to be one inch. Fig. 6 is an example of this group. Note the angulation of the third portion of the duodenum as well as at the duodenojejunal flexure. Fig. 7 demonstrates a clinical case which could be classified in the same group. Here the intestinal decompression tube as it passes through the third portion of the duodenum passes from right to left and upward. The upward obliquity is not as acute as in those patients in Group 1. It will be seen that there is no kinking of this tube anywhere along its course. Fig. 8 demonstrates a third portion of the duodenum which is classified in the same group. Here a moderately acute upward obliquity of the third portion of the duodenum is noted. Notice, however, the very acute angle at the duodenojejunal flexure and the definite kink in the intestinal tube at that point as a result of this acute angle. This patient was intubated for intestinal distention, the result of a paralytic ileus, as a result of diffuse peritonitis. There was tremendous distention.

Fig. 6.—The upward angulation of the second portion of duodenum is not as acute as in Fig. 4. Ligament of Treitz is longer.

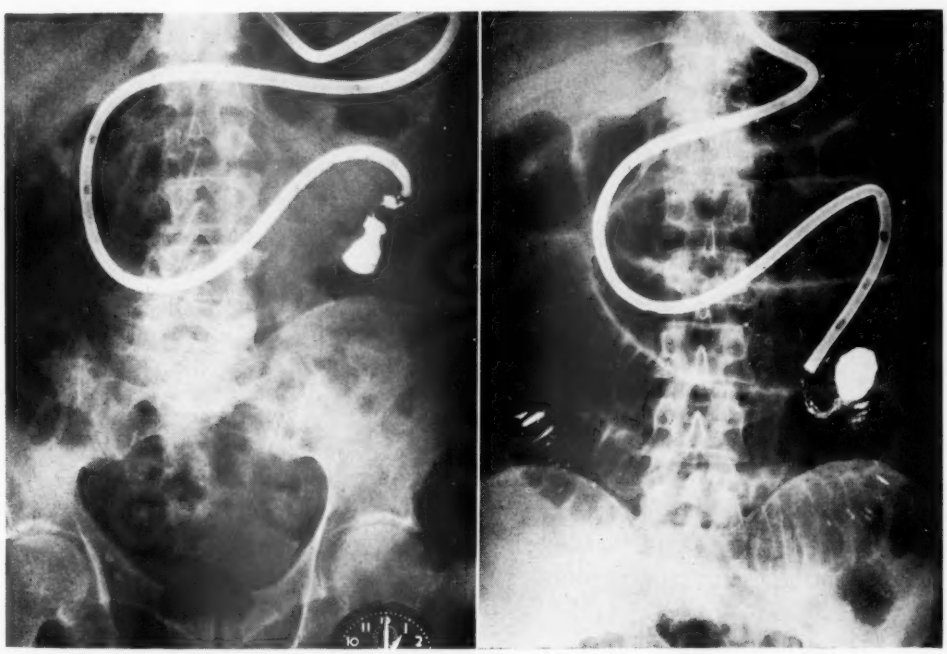

Fig. 7. Fig. 8.

Fig. 7.—Note angulation of the third portion of the duodenum and at the duodenojejunal flexure. All angulations are not acute.

Fig. 8.—The arc at the angle between second and third portions of the duodenum. There is an acute angle at the duodenojejunal flexure, a kink in the intestinal tube at that point, and marked intestinal distention in this case.

In cases of this type the proximal jejunum becomes heavily weighted with fluid as well as gas. The weight of this jejunum causes an acute angulation at the duodenojejunal flexure as noted in this figure. These patients are always difficult to intubate. Ambulation in this patient resulted in a successful passage of the tube beyond the flexure as noted here.

SUMMARY

In a study of all patients intubated during the past five years and an anatomic study of the duodenojejunal flexure of thirty-five cadavers, certain fundamental observations could be made. The relationship that exists between the length of the ligament of Treitz and the acuity of the angles formed by the second and third portions of the duodenum as well as between the duodenum and jejunum may be of the greatest importance in insuring a successful intubation in cases of paralytic ileus.

It has been possible to divide all these cases into three groups with respect to the angulation of the third portion of the duodenum. In the first of these groups, the direction taken by the third portion of the duodenum in its passage from right to left is horizontal. In this type of case the duodenojejunal flexure is not acute or may even be nonexistent. Such patients are very easily intubated and an arrest of the intestinal decompression tube at the duodenojejunal flexure is never caused. This group was found to constitute 23 per cent of the cadavers dissected. In these cases the ligament of Treitz was found to be long. The length of the ligament of Treitz ranged from two to two and one-half inches in all these cases.

In the second of these groups, there was a well-marked acute angulation of the third portion of the duodenum in its passage from right to left to the duodenojejunal junction. In this group the ligament of Treitz was invariably found to be short, ranging in length from one-half to three-quarters inch. Invariably in this group the angle formed at the duodenojejunal flexure was found to be so acute that a definite kink could be noted in the intestinal tube. In tubes of small luminal diameter, such a kink might well occlude the lumen. Patients in this group were by far the most difficult to intubate beyond the duodenojejunal flexure, particularly in cases of paralytic ileus. The downward pull of the heavily weighted proximal jejunum in such cases increased the angulation at the duodenojejunal flexure as almost completely to occlude the bowel. Successful intubation was invariably obtained by turning the patient upon the left side for a period of time to permit the mercury-containing balloon-tipped tube to run downhill to the duodenojejunal flexure. From that point ambulation was necessary to insure further progress of the tube. In innumerable instances an arrest of the intestinal tube at the duodenojejunal flexure has been demonstrated in this type of case. In all such cases ambulation of the patient was essential for successful intubation. This group constituted 43 per cent of all cadavers dissected.

Group 3 constituted 34 per cent of all cadavers dissected. In this group the angulation of the third portion of the duodenum and the duodenojejunal flexure occupied an intermediary position between Groups 1 and 2. The ligament of Treitz was found to be one inch long. In this group the junction between the

second portion of the duodenum and the third portion was not nearly as acute as in Group 2. The intestinal tube in traversing the duodenum of this type of case showed no tendency to kink. Most of the patients in this group were successfully intubated with ease. Occasionally in a patient suffering from paralytic ileus with a heavily weighted proximal jejunum the angulation at the duodenojejunal flexure was made so acute as to impede the further downward progress of the intestinal tube.

If the patient to be decompressed has little impairment of the propulsive mechanism of the gastrointestinal tract, then the angulation at the ligament of Treitz is of little importance. Peristaltic activity in such cases would readily propel any intestinal tube beyond this point. The great importance of a short ligament of Treitz with a concomitant acute angulation at the duodenojejunal flexure is found in cases of atony of the bowel or paralytic ileus in which there is a markedly impaired intestinal motility. In such cases a heavily weighted proximal jejunum pulling upon the short ligament of Treitz could effectively obstruct the intestinal stream. Since it is such cases that need intestinal intubation the most, the importance of any method of overcoming this barrier should be evident.

CONCLUSION

1. The ligament of Treitz was found to range from one-half inch to two and one-half inches long.

2. The length of the ligament of Treitz appeared to be associated with a variation in the angulation of the third portion of the duodenum and the duodenojejunal flexure.

3. Patients with a short ligament of Treitz were found to present a very acute upward angulation of the third portion of the duodenum and an acute angulation at the duodenojejunal flexure. This acute angle often constitutes a barrier to successful intubation.

4. Patients with a long ligament of Treitz present no problem to the intubator as the third portion of the duodenum was found to be horizontal and the duodenojejunal flexure not acute.

5. The angulation at the duodenojejunal flexure in patients with paralytic ileus is of the greatest importance as the downward pull of the weighted proximal loop may obstruct the bowel at that point.

I should like to express my appreciation to Professor Collings of Wayne University for putting at my disposal the anatomic material used.

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COMPOUNDS OF ZIRCONIUM FOR X-RAY MEDIA

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IN AN attempt to produce a substance which would render brain tumors radiopaque, many elements and compounds have been investigated in our laboratories. As previous investigators have shown that the electrochemical charge of an ion determines whether or not it crosses the blood-brain-barrier, special attention has been paid to this aspect of the compounds used. Broman[1] has shown that under normal conditions only positively charged ions pass through the blood-brain-barrier into the brain substance. On the other hand, in the presence of a brain tumor or any local pathologic process, the protective mechanism of the blood-brain-barrier is altered. This allows the accumulation of negatively charged ions in the involved area.

One of the substances investigated, zirconium, element number 40 with an atomic weight of 91.2, was found to be relatively nontoxic when injected intraperitoneally in mice, and was also found to be more radiopaque than would be suspected. Accordingly, barium, iodine, lead, and zirconium were compared in equal percentage and molar solutions in a series of test tubes. X-ray film in a cardboard holder was used; the radiographic factors were: 100 milliamperes, 1 second, and 40 kilovolts. The zirconium solution was found to be more opaque than equal amounts of barium or iodine, and approached the opacity of lead (see Fig. 1).

Sodium zirconyl citrate was made after the method of McClinton and Shubert[2] with the hope that in placing the zirconium in an anion state the normal blood-brain-barrier would not be penetrated, but that areas of altered physiology in the barrier would permit the zirconium compound to collect and become radiopaque. Thus far we have not been able to demonstrate a brain tumor by x-ray with this technique.

However, when sodium zirconyl citrate was injected intravenously into a rabbit (dosage .7 Gm. per kilogram of body weight), it was noted that the substance was being excreted rapidly by the kidney, and that an x-ray picture of the kidney parenchyma resulted (see Fig. 2). The substance can be found by x-ray examination in the kidneys for one hour after the injection. The radiographic factors were 10 milliampere seconds and 46 kilovolts. Since impure materials were used in the synthesis of the final product, the toxicity necessarily precludes its practical application at the present time.

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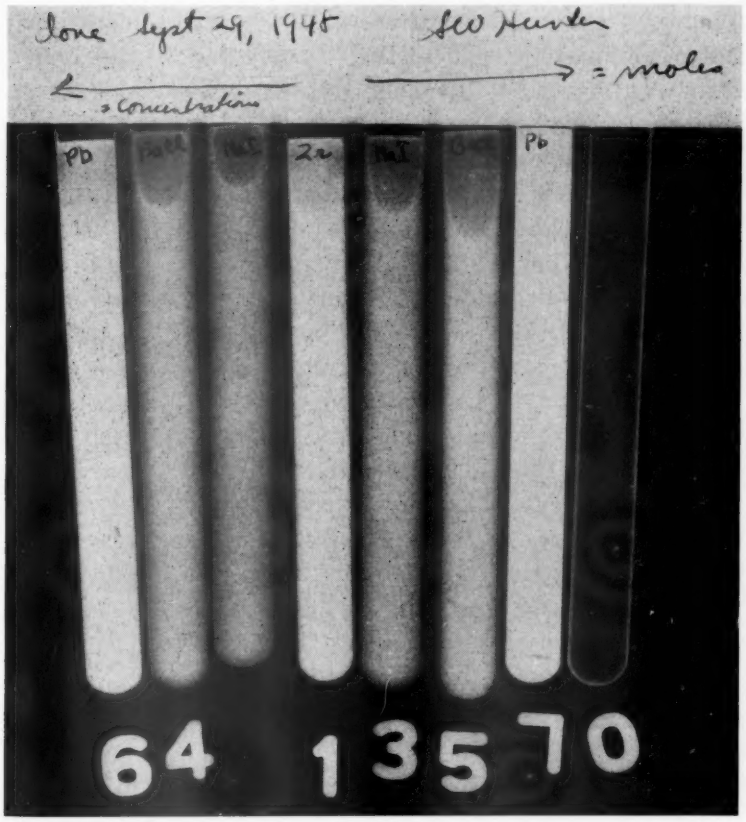

Fig. 1.

Fig. 2.

Fig. 1.—X-ray picture comparing zirconium, barium, iodine, and lead. The left portion of the picture represents equal concentrations of lead, barium, and iodine compared with an equal concentration of zirconium. The right portion represents molar solutions of iodine, barium, and lead compared with an equal molar solution of zirconium.

Fig. 2.—This is an x-ray film of a rabbit ten minutes after injecting sodium zirconyl citrate (.7 Gm. zirconium per kilogram body weight of rabbit). Note that the left kidney is partially hidden by the rib cage and spinal column.

The toxicity of the substance was worked out in mice by injecting varying doses intraperitoneally. The lethal dosage for 50 per cent of the mice was 2.7 Gm. per kilogram. However, this toxicity level does not hold true when the injection is made intravenously. The exact level for the lethal dosage for 50 per cent when the chemically pure material is used intravenously has not yet been determined, but it is believed from the experiments already done that it will be in the order of magnitude of one-fourth the intraperitoneal lethal dosage per 50.

There are occasions in the management of bowel lesions when the surgeon and radiologist would like to use a radiopaque medium for study but have serious misgivings over employing barium sulfate because of the known tendency of that medium to inspissate in the bowel in partially obstructing lesions. Also, there are times when fistulas are suspected and the barium is then withheld due to its deleterious effect when free in the intraperitoneal space. In these situations a solution of zirconium might be used to advantage. Satisfactory x-ray pictures of the dog's gastrointestinal tract have been made with sodium zirconyl citrate, and zirconium oxide. None of the zirconium compounds used were later found in the blood or urine. Practically 100 per cent of the compound was excreted from the bowel in five to six hours.

There is reference in the literature to zirconium oxide being used as an opaque medium, but the procedure was patented[2] by the investigator and there has been no further use made of the method.

At the present time other methods and other zirconium compounds are under study in our laboratories.

Acknowledgment:—The zirconium compounds used in these experiments were supplied by the Titanium Alloy Manufacturing Division of the National Lead Company.

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Case Reports

HEMANGIOMA OF THE BREAST

Report of Case

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ANGIOMAS of the breasts are extremely rare. The lesion concerned in this study is of interest because of its location, its rarity, and its failure to respond to radiation therapy. In a series of 5,570 breast tumors reviewed by Smythe,[1] only 23 hemangiomas were found, comprising a percentage of 0.004 per cent. There are two types of breast hemangiomas, the capillary and cavernous. The case reported in this study falls into the latter group. The majority of these tumors are benign, although some are malignant. The ratio of those occurring in females to those in males, in the study of Smythe,[1] was 10.5 to 1. The majority of the patients were in the 20 to 40 age group. According to Geschickter,[2] mammary hemangiomas are usually of the cavernous type. They are nonencapsulated, subcutaneous tumors usually found in the young or middle ages. On palpation the tumors are semifluctuant and cast a shadow on transillumination. There is one distinguishing feature between this lesion and the intracystic papilloma or papillary carcinoma, namely, the absence of a sanguineous discharge from the nipple, for in the former case, the vascular spaces are not connected with the mammary ducts. Final diagnosis, however, cannot be made until exploration and study of the tissue are made by microscopic means.

Sherry[3] felt that a unilateral tumor of the breast that increases rapidly in size, decreases in volume on compression, only to return rapidly on relaxation, which may or may not have a bruit or thrill, all should be suggestive of this lesion. A variety of treatments has been used for these tumors but in reviewing the literature and in the light of our experiences we feel that surgery is indicated. In those cases in which the tumor is small, a local excision may be carried out and for the more extensive cases, a mastectomy should be done.

REPORT OF CASE

A married white woman, aged 23 years, was first seen by one of us (G. F. M.) on Jan. 3, 1948, stating that she had a "birthmark" on the right breast which had enlarged in the past few months. The remainder of her history was essentially negative. She was the mother of two children and stated that the right breast had increased in size out of proportion to the left with each of her two pregnancies.

Physical examination was essentially negative, save for a tumor with a small eroded area in the dome, involving the upper half of the right breast. It decreased in size on compression and rapidly refilled when the pressure was released. There was no evidence of a bruit or thrill and the tumor transilluminated light poorly. A diagnosis of hemangioma was made and radiation therapy was recommended. Accordingly the patient was referred to a

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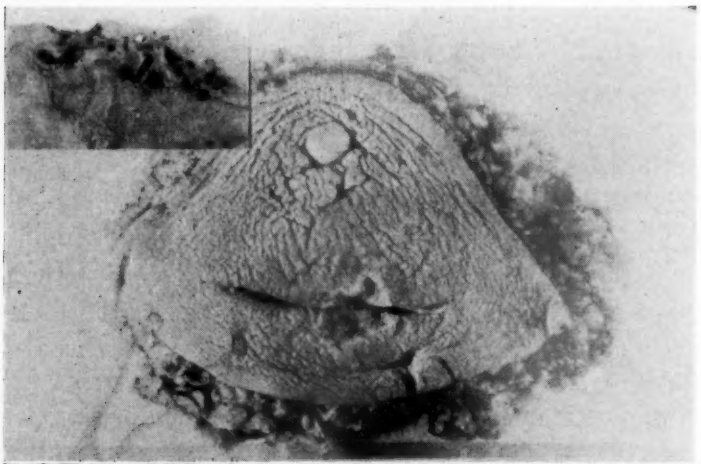

Fig. 1.

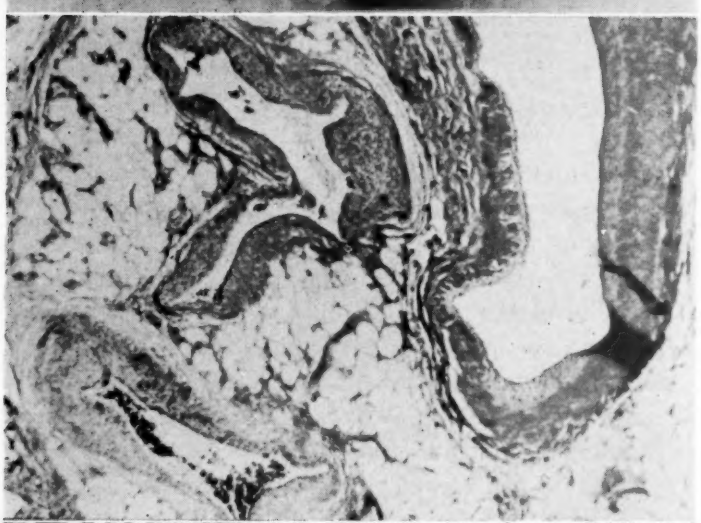

Fig. 2.

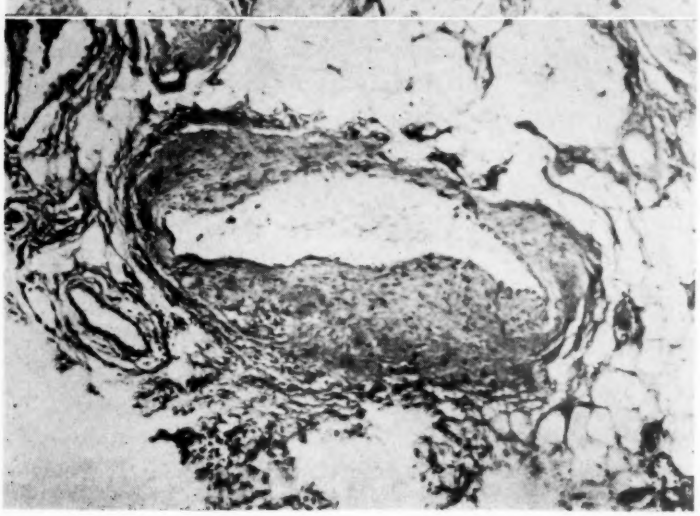

Fig. 3.

Fig. 1.—The gross specimen of breast with the cutaneous ulcer. The inset in the left upper corner is a cross section through the hemangioma. It demonstrates the size and distribution of the blood vessels. (Breast and hemangioma reduced one-third actual size.)

Fig. 2.—A typical field in the tumor. Distorted blood vessels are seen in a somewhat fatty stroma. Intimal proliferation has thickened the vessel walls. (Hematoxylin and eosin ×33.)

Fig. 3.—A higher magnification of a single vessel which shows the effect of the x-ray therapy. About one-half of the lumen was obliterated by the intimal proliferation. (Hematoxylin and eosin ×100.)

roentgenologist who carried out a series of treatments over the next seven months. The patient again reported to one of us (G. F. M.) on Aug. 20, 1948, stating she had had five courses of x-ray therapy without benefit and that it was her feeling that the lesion had progressed. On one occasion, the lesion bled profusely and it was necessary to insert Gelfoam to control this hemorrhage.

Examination on the second visit revealed an increase in the size of the tumor and a large ulcer over the dome. A dry gauze pressure dressing had been applied to control the ooze. There was no evidence of glandular involvement. Mastectomy was recommended. This was carried out on Aug. 23, 1948. At the time of surgery there was no gross evidence of malignancy. The patient's convalescence was uneventful.

The report of the gross and microscopic pathology was made by one of us (L. R. H.) and is as follows:

Gross.—The specimen was composed of a breast which measured 15 cm. in its greatest dimension. An ulcer 3 cm. across was present lateral to the nipple. A cut through this ulcer revealed many large caliber blood vessels mixed with fibrous tissue and fat. The largest vessel measured 1 cm. in diameter and was still blood-filled. The vascular tumor measured 8 by 7 by 6 cm. in its gross dimensions.

Microscopic.—Sections showed a vascular tumor lying under the skin. Starting at the surface, a cutaneous ulcer was encountered first. The crater was filled in with necrotic tissue and an exudate made up of numerous lymphocytes and large mononuclear cells and fewer eosinophils. Within 1 mm. of the surface, the first large caliber vessels were seen (Fig. 1). Extensive intimal proliferation was noted, and at this superficial level, the vessel walls were infiltrated with inflammatory cells similar to those seen in the ulcer crater. The deeper vessels did not show this exudate.

Study of the individual vessels indicated that they were for the most part dilated capillaries. A few of the larger vessels showed scattered muscle fibers but no elastic tissue. These latter vessels were interpreted to be small venules. The typical vascular channel, however, contained blood, was lined by a single layer of endothelium, and the rest of the wall was then made up of young connective tissue, the result of the intimal proliferation. In some of the smaller vessels complete obliteration had occurred. The endothelial cells showed no evidence of a malignant change.

The supporting stroma was either fibrous or fatty. Near the surface the stroma was infiltrated by numerous lymphocytes and eosinophils. Near the edges of the tumor, small capillaries were occasionally encountered which showed a perivascular lymphocyte collar. These capillaries were considered nutrient vessels of the stroma and not a part of the hemangioma. No breast ducts were observed admixed with the tumor.

The overlying skin showed a few changes perhaps due to the x-ray therapy. The cells of the epidermis exhibited pyknosis of nuclei and frequent vacuoles in the cytoplasm. In the immediate subadjacent dermis, numerous small capillaries could be seen lined with swollen endothelial cells. Pigment was also increased in amount and was found within chromatophores lying in the dermis.

CONCLUSIONS

1. The diagnosis of a hemangioma is based on the presence of a unilateral tumor of the breast that increases rapidly in size, decreases in size on compression, refilling rapidly on relaxation, and which may or may not have a bruit or thrill.

2. Surgical removal is the treatment of choice, local excision for small lesions and mastectomy for the larger ones.

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INTESTINAL LIPODYSTROPHY OR WHIPPLE'S DISEASE

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WHIPPLE,[1] in 1907, reported a case characterized by deposits of fat and fatty acids in the intestinal and mesenteric lymphatic tissues associated with cachexia and arthritis. This case represented a disease previously undescribed which has since become known as intestinal lipodystrophy or Whipple's disease. No other cases were reported for sixteen years, until Blumgart[2] described three cases in 1923. In the fifteen years that have elapsed since 1923, fifteen cases, excluding the one herein described, have been reported. The logical explanation for this increased incidence appears to be the dissemination of knowledge about the syndrome among members of the profession. Cases have been reported by Whipple,[1] Blumgart,[2] Fleischmann,[3] Jarcho,[4] Hill,[5] Boeck,[6] Reinhart and Wilson,[7] Korsch,[8] Pearse,[9] Sailer and McGann,[10] Apperly and Copley,[11] Fitzgerald and Kinney,[12] Pemberton, Comfort, and Fair,[13] Rosen and Rosen,[14] Amsterdam and Grayzel,[15] Collins and Berdez,[16] and there is a case reported in this paper.

Whipple's case was that of a physician and was characterized clinically by: gradual loss of weight and strength, stool consisting chiefly of neutral fat and fatty acids, being white and creamy, indefinite abdominal pain, and a peculiar multiple arthritis. These symptoms and signs are not very characteristic of any particular syndrome, but the pathologic findings were unique and Whipple's classical description has not been improved upon to date. The gross changes in the mesenteric lymph nodes were most marked, the nodes being very large, measuring 3 to 4 cm. in diameter, and very elastic to the touch. On section, they appeared to be a pale yellowish color with virtually total disappearance of lymphatic tissue, which was replaced by neutral fat and fatty acids. There was also present a chronic inflammatory reaction associated with many giant cells. The intestinal mucosa showed enlargement of the villi caused by large deposits of neutral fat and fatty acids in the lymph spaces and an infiltration of the glandular tissue by large mononuclear giant cells. The submucosa showed similar changes. The jejunum revealed a pink or red velvety swollen mucosa which was flecked with little pin-point, yellowish grains that seemed to be intimately connected with the mucosa and in some cases beneath it. Peyer's patches were not conspicuous. The large intestine showed a smooth, pale mucosa. The lymphatic tissue of the bronchial glands, bone marrow, and lungs showed no abnormalities of importance. In our case the villi and crypts of the small intestine showed marked thickening of the mucosa. The mucosa and submucosa contained sheets of foam cells, mononucleated and multinucleated giant cells, and large clear vacuoles repre-

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senting fat droplets. In some areas there was infiltration with polymorphonuclear leucocytes. Fat stains with Sudan 4 on formalin-fixed tissue showed large and small fat droplet deposits in the foam cells and giant cells.

Since the first case reported by Whipple,[1] names other than intestinal lipodystrophy have been applied to the syndrome. Among these are: lipophagia granulomatosis, lymphadenocele, mesenteric chyle adenectasis, and lymphadenectasis. However, from present-day knowledge of the disease, the term intestinal lipodystrophy appears to be the most adequate.

CASE REPORT

A 47-year-old white man entered Touro Infirmary in January, 1934, with a complaint of pain in the arms and ankles. This pain had been present for the past seven months and stiffness in both ankle and wrist joints was present. His weight was 168 pounds. Diseased tonsils and marked dental caries were noted. The heart was enlarged to the right and an occasional ectopic beat was present. The diseased teeth were extracted and tonsillectomy was done.

In January, 1938, the patient again returned to the clinic with a chief complaint of pain in the wrists, ankles, back, and cramps in the stomach. This attack had begun three weeks previously when the patient noted a severe cramping pain in the epigastrium. There was much belching and a large amount of gas was passed per rectum. The pain disappeared and reappeared after symptom-free periods of three to four hours. It usually began in the epigastrium and radiated to the entire abdomen. It was not related to any particular type of food but did tend to appear three to four hours after meals. At the time of admission the patient was constipated and required either epsom salts or castor oil. The stools were essentially normal in color and consistency. Social history revealed the patient to be a truck driver. He did not use alcohol and smoked occasionally.

In February, 1942, the patient underwent an appendectomy. The recovery was uneventful. He returned to the clinic in April complaining of a low back pain. In orthopedic clinic, it was stated that the signs and symptoms were pathognomonic of hypertrophic arthritis of the lumbosacral spine.

The patient was not seen again until September, 1945, when he entered the hospital with a chief complaint of diarrhea and three to seven stools a day for two years. In the interim period of two years, his weight had dropped from 180 pounds to 110 pounds. There was no fever, nausea, anorexia, vomiting, jaundice, or intolerance to fat or other foods. The stools were brown and showed no evidence of discoloration. X-ray examination of the gastrointestinal tract and lungs while in the hospital at this time were essentially negative. The statement was made in the progress notes that the patient was an emaciated, barrel-chested man in no acute distress. The skin was slightly jaundiced, swarthy, and dry. The tongue was smooth, shiny, and red with several darker red macules. The patient was suffering from a hypoproteinemia as well as anemia. In the hospital he was treated with blood transfusions, parenteral vitamins, and an adequate diet. The diarrhea continued for some time and then subsided. A proctoscopic examination revealed an angry, red, edematous, friable bowel with some spasm. No ulcerations were noted. Following the diet and vitamin therapy, he was discharged as improved. The condition was believed to have been due to malnutrition. It was also believed in view of the diarrhea and the shiny red tongue that the patient was suffering from sprue. Gastric analysis revealed a free hydrochloric acid of 6°, total acid of 27°, serum proteins varied from 4.3 to 5.8 Gm. per 100 c.c. Albumin-globulin ratio was 2.88 and 2.74. Repeated stool cultures were negative for pathogens of typhoid or dysentery group. The feces were gray and soft and contained no blood, parasites, or ova. Red blood cells varied between 2.2 million and 3.05 million, white cells between 13,000 and 10,000. In November, the patient had a bilateral varicose vein ligation with uneventful recovery.

The patient returned to the clinic in February, 1946, complaining of fourteen pound weight loss. He noted weakness, loss of appetite, nervousness, and dyspnea. Gastric analysis

revealed free acid 46°, total acid 60°. His weight on Oct. 19, 1946, was 131 pounds. On Dec. 7, 1946, the patient had diarrhea for two weeks with three to five bowel movements daily. These were loose and watery. No blood or mucus was noted. Peripheral blood study Dec. 13, 1946, revealed 78 per cent hemoglobin, 3.8 red blood cells, 12.1 Gm. hemoglobin. Re-examination of stools failed to reveal parasites or ova.

He was admitted to the hospital about this time because of a salivary calculus. He was 55 years old. For two months he had a complaint of pain in the epigastrium radiating to the abdomen. The pain was not related to food intake. For three weeks, he had a diarrhea of three to five stools a day. There was no blood or mucus. The face was sunken, the skin was loose and dry. There was loss of skin turgor. The teeth were carious. A hard lobulated mass could be palpated in the submaxillary region on the right side at the base of the tongue. Jugular pulsations were visible. Extrasystoles were noted. When the heart was examined a bradycardia of 61 per minute was recorded. The abdomen was believed to be rather large for a person who appeared as emaciated as this patient. Loud borborygmi were heard. Ankle edema was present. Barium enema revealed no organic lesions of the bowel. The diarrhea subsided tempoarily following this procedure. It recurred within a few days and repeated stool cultures were negative for pathogenic organisms. On Jan. 4, 1947, the patient had eleven bowel movements in twenty-four hours. On Jan. 6, 1947, proctoscopic examination revealed a smooth inflamed nongranular mucosa. Vitamin therapy was instituted. The diarrhea was believed to be on a deficiency basis. He was given a high carbohydrate, high protein, low fat diet. The hemoglobin rose to 12.5 Gm. per 100 c.c., the serum proteins were 5.11 Gm. per 100 c.c. He gained 1½ pounds in the hospital. On Jan. 13, 1947, proctoscopy revealed definite improvement in the appearance of the mucous membrane. The diarrhea was also somewhat improved. On Jan. 14, 1947, the patient stated he had five bowel movements.

On Jan. 16, 1947, he had severe cramps. He was very depressed and anorexic. He vomited water frequently but the abdomen was not distended. There was no pain or tenderness and the previously mentioned peristalsis could no longer be heard. On Jan. 18, 1947, the patient's abdomen was distended. Flat plate showed no fluid levels but there was marked gaseous distention. On Jan. 19, 1947, under spinal anesthesia, a portion of the ileum was found to be gangrenous and was resected. An end-to-end anastomosis was performed. A diffuse peritonitis was noted. Mesenteric thrombosis was the preoperative and postoperative diagnosis. Following operation, he developed a gallop rhythm and rapid digitalization was accomplished. On Jan. 20, 1947, the blood chlorides were 390 mg. per cent, CO_2 combining power, 57 volume per cent. On the second postoperative day the patient's condition was very poor: temperature 103° F., pulse weak and thready. He was cyanotic and died at 7:50 A.M. on Jan. 21, 1947.

Stool examinations while in the hospital were done repeatedly and showed moderate to large numbers of fatty acid crystals and a few yeast forms. No parasites or ova were found. The stools were usually light to yellow in color, frequently liquid, and fatty in appearance. Gastric analysis revealed free acidity of 18° and a total acidity of 24°. The red blood cells varied from 4 million to 3.6 million, the white blood cells from 6,000 to 13,000, serum proteins varied from 51.11 to 7.49. Repeated stool cultures were negative. Gastrointestinal series at various intervals were not diagnostic of organic disease.

PROTOCOL

General Body Description.—This was the body of a fairly well-developed and well-nourished white man appearing 55 years of age. There was no discharge from the nose or mouth. The pupils were equal and 3 mm. in diameter. The chest was symmetrical. The abdomen was distended and had a midline longitudinal incision 20 cm. in length. The skin was unsutured and gauze had previously been packed into the wound. The upper and lower extremities were symmetrical.

Skull and brain: The skull and brain were not examined.

Internal examination: The peritoneal cavity contained approximately 1,200 c.c. of a dirty reddish-gray exudate. The loops of small intestine were covered with a fibrinopurulent exudate and were distended.

Pleural cavities and lungs: There was approximately 20 c.c. of serous yellow fluid in each pleural cavity. Bilateral apical adhesions were present. The right lung weighed 310 grams. The lower lobe was atelectatic, and one section revealed a beefy red surface. The upper and middle lobes were reddish-gray, crepitant, and one section revealed a moist red surface. No emboli were present in the pulmonary artery or its branches. There was a small amount of mucoid material in the bronchial tree. The left lung weighed 200 grams. The left lower lobe was atelectatic. The upper lobe was similar to that of the right.

Pericardial cavity and heart: The pericardial cavity contained 20 c.c. of yellow fluid. There was definite left ventricular hypertrophy. The heart was opened to reveal a glistening pink endocardium. There was no fibrosis or ulceration of the valves. The coronary arteries were serially sectioned and no thrombosis was found. The myocardium presented a reddish-brown cut surface showing minute gray scarred areas.

Liver: The liver weighed 2,100 grams. A fibrinopurulent exudate covered Glisson's capsule. The organ sectioned to reveal a reddish-brown surface.

Gall bladder: The gall bladder contained approximately 15 c.c. of dark green tenacious bile. No stones were present.

Spleen: The spleen weighed 260 grams. It presented a soft purplish red trabeculated surface.

Pancreas: The pancreas was of normal size and shape. It sectioned to reveal a yellow lobulated surface.

Adrenals: The adrenals showed a bright yellow cortex and gray medulla.

Kidneys: The right kidney weighed 150 grams. Its capsule stripped with ease to reveal a finely granular reddish-brown surface. Several cortical retention cysts 2½ cm. in diameter and containing a clear yellow fluid were present. The organ sectioned to reveal a brown medulla. The renal calices and pelvis were not dilated and the ureter was patent. left kidney weighed 150 grams. The description was similar to that of the right.

Bladder: The mucosa showed several focal submucosal hemorrhages.

Prostate: The prostate was not enlarged and sectioned to reveal a moist grayish-white surface.

Gastrointestinal tract: The gastrointestinal tract was removed and opened. The mesentery was markedly thickened and edematous. At the time of autopsy no gross enlargement of lymph nodes was noted and therefore no sections of mesenteric nodes were taken. The serosa of the mesentery and bowel was covered with friable gray exudate. The bowel was distended up to the anastomotic site, which was well closed and showed no evidence of leakage. The remainder of the small bowel was collapsed. The large bowel was slightly distended with gas. The small intestine was opened to reveal a thickened, velvety mucosa showing prominent yellow villi that were greasy in appearance and consistency. The mucosa and submucosa were thickened and edematous. These changes extended from the jejunum to the cecum. Several superficial mucosal ulcerations in the cecum and ascending colon were noted; these varied in size from a few millimeters to 1 cm. in diameter.

Special Procedures.—Culture was taken from the peritoneal cavity. Smear showed gram-negative bacilli. Culture (final report) showed *Bacillus coli, Aerobacter aerogenes,* and alpha hemolytic streptococci.

Microscopic Findings.—Sections of adrenals and pancreas showed nothing of pathologic significance. Sections of lung, liver, and spleen showed congestion.

Heart: There were scattered foci of fibrosis. The myocardial fibers were slightly hypertrophied.

Kidneys: There were several retention cysts surrounded by zones of fibrosis containing atrophied tubules, hyalinized glomeruli, and infiltrated with chronic inflammatory cells. There were foci of subcapsular fibrosis containing atrophic tubules and infiltrated with round cells. Hyalinized glomeruli were quite frequent throughout the sections. There were moderate arteriolar changes.

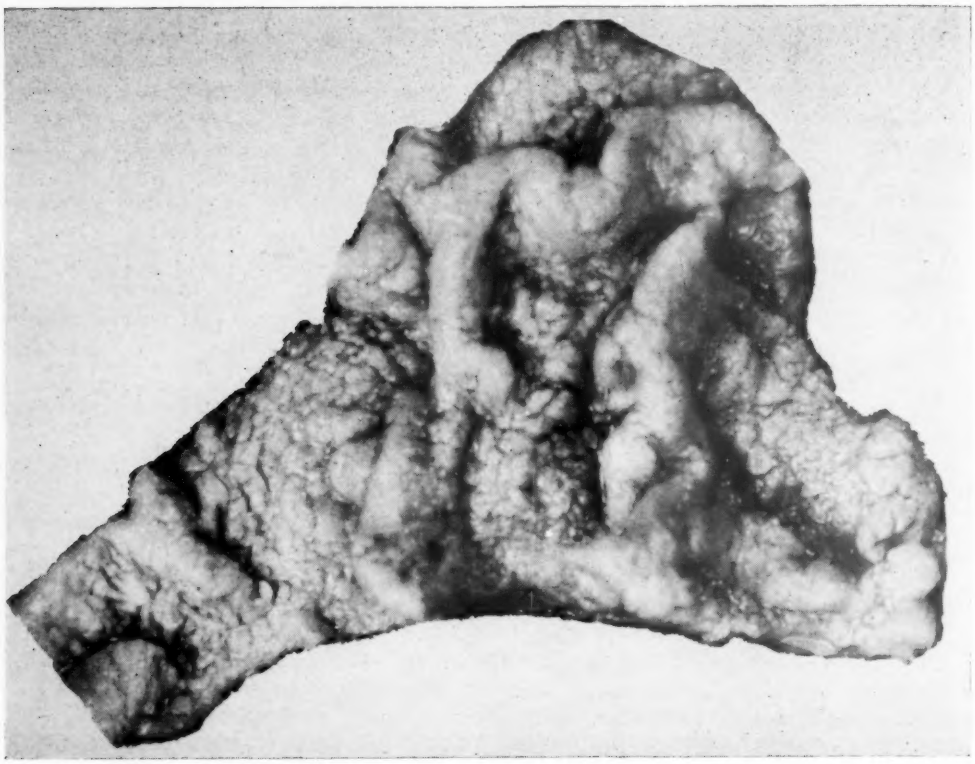

Fig. 1.—Segment of upper ileum showing prominent villi of greasy consistency.

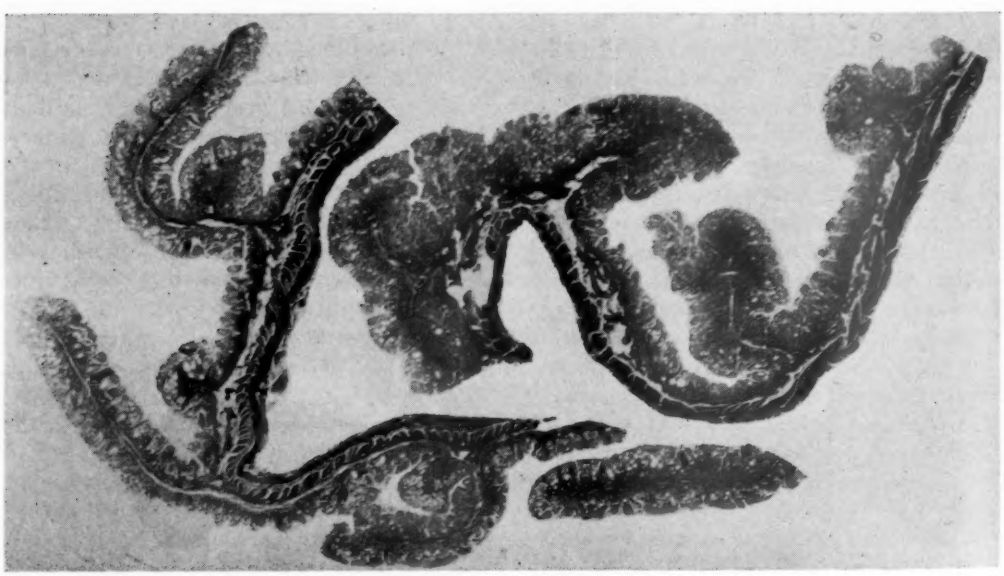

Fig. 2.—Micro-Summar showing relief outline of enlarged villi.

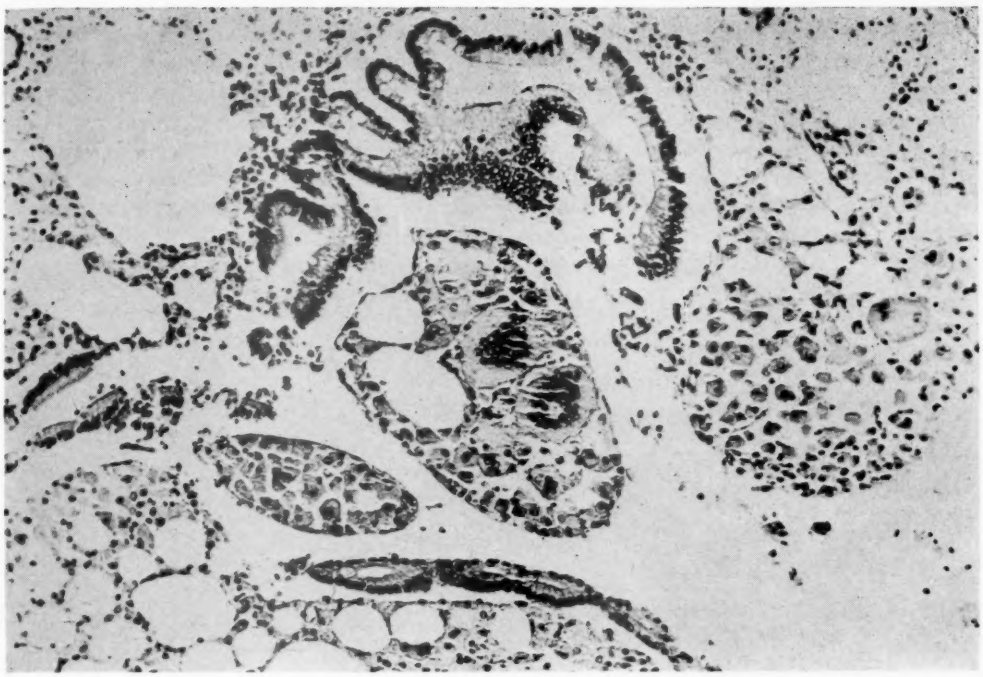

Fig. 3.—Engorgement of villi with mononucleated and multinucleated foam cells and fat droplets (×100).

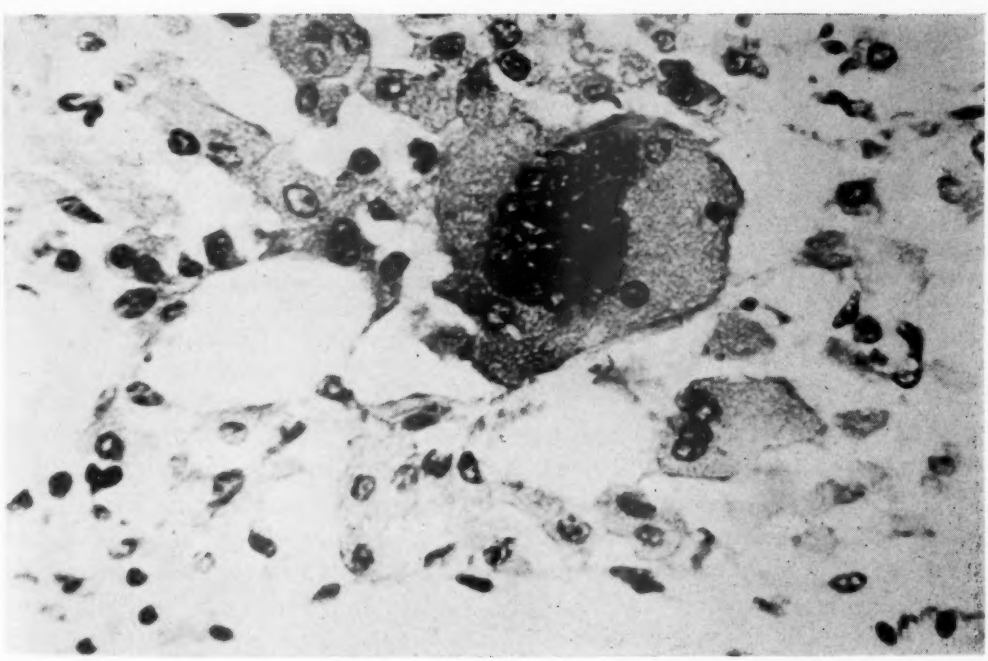

Fig. 4.—Multinucleated giant cell and foam cell detail (×400).

Gastrointestinal tract: Sections of small intestine showed marked hypertrophy of the villi with thickening of the mucosa and submucosa. The villi and crypts were lined with a normal-appearing tall columnar epithelium. The mucosa and submucosa contained sheets of foam cells, mononucleated and multinucleated giant cells, and large clear vacuoles representing fat droplets. In some areas there was infiltration with polymorphonuclear leucocytes. The muscularis was edematous. The serosa was covered with a fibrinopurulent exudate and there was subserosal edema and infiltration with acute inflammatory cells. Fat stains with sudan IV on formalin-fixed tissue showed large and small fat droplet deposits in the foam cells and giant cells. Sections of colon show several foci of mucosal hemorrhage.

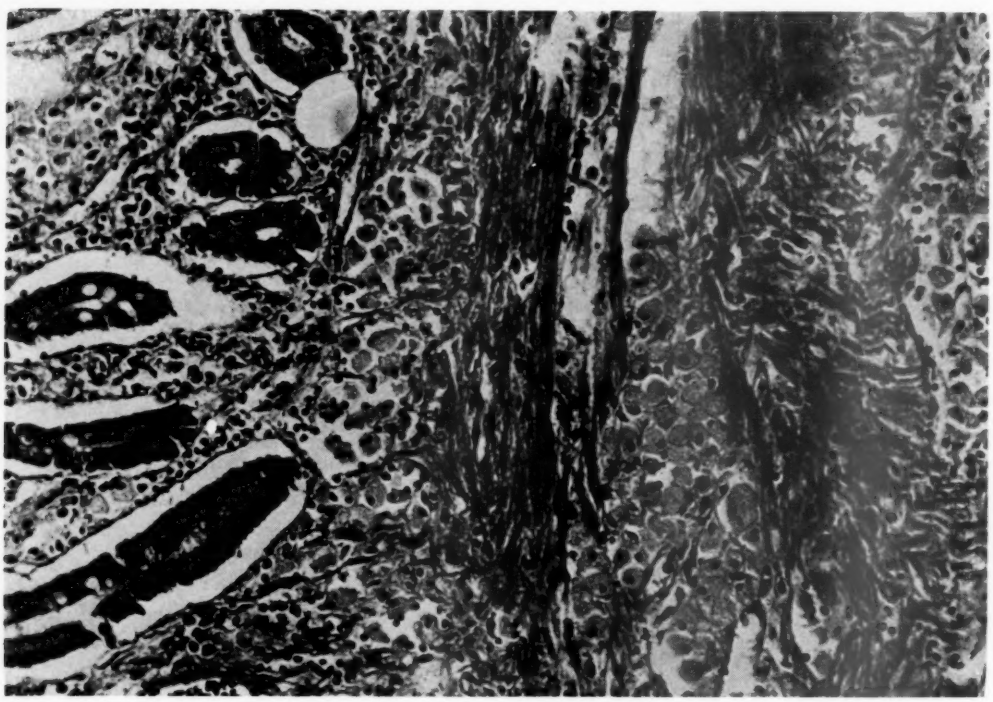

Fig. 5.—Foam cells in submucosa (×100).

Final Anatomic and Microscopic Diagnoses.—The diagnoses were (1) intestinal lipodystrophy (Whipple's disease); (2) peritonitis, subacute, progressive, due to (3) *B. coli, A. aerogenes,* and alpha hemolytic streptococci; (4) atelectasis, bilateral; (5) benign nephrosclerosis; (6) chronic pyelonephritis; (7) retention cysts, multiple of kidneys.

SUMMARY OF CASE

The long-standing history of undiagnosed diarrhea, abdominal discomfort, and anemia along with the gross and microscopic examination make up a typical picture of intestinal lipodystrophy. Death was attributed to a diffuse peritonitis. In retrospect the same intestinal lesions were found in the distal and proximal ends of the infarcted bowel removed at surgery.

COMMENT

With the report of cases since 1923, more data about the clinical aspect of the disease have become available. Males are usually affected from the fortieth to the sixtieth year of life. They generally complain of some vague

gastrointestinal symptoms such as fullness, bloating, and discomfort following the intake of food. Hypotension is usually present. The systolic pressure of the patient reported in this instance was 104. A small percentage developed polyarthritis as our patient did. Other than these symptoms, very few early manifestations occur. The patient is often labeled a psychoneurotic. However, as time passes a fatty diarrhea appears. The stools may be creamy and foamy in appearance, occur four to five times a day, and at times are blood-streaked. This blood may be due to minute ulcerations in the small intestine. Later such findings as anemia, wasting, and mild jaundice may be noted. Gastrointestinal series and gall bladder visualization are usually negative. Stool analysis reveals a marked excess of neutral fat and fatty acids. Gastric analysis will frequently show an achlorhydria. A hypocalcemia has been reported in some cases and may cause symptoms of tetany. This finding is especially interesting, for hypocalcemia and tetany have been noted in some cases of acute pancreatitis, yet the pancreas at autopsy in intestinal lipodystrophy does not appear to be involved.

The differential diganosis is most difficult and until 1945 no antemortem diagnosis had been made. Pearse made the first antemortem diagnosis when he removed the mesenteric nodes at an exploratory operation, and microscopic examination revealed the true diagnosis. Incidentally, this diagnosis was confirmed by Whipple,[1] who examined the specimen. The usual diagnoses that had been made previous to autopsy were: sprue, Hodgkin's disease, tetany, regional ileitis, colitis, Boeck's sarcoid, and pancreatic insufficiency. The diagnosis is generally made at autopsy, as happened in this case.

There has been very little information added concerning the gross pathologic abnormalities described by Whipple.[1] The essential pathologic changes occur in the small bowel and in the mesentery. The mucosa of the jejunum and ileum is largely replaced by fat-filled macrophages or foam cells. Whipple[1] stated, "The villi of the small intestine were enlarged by droplets of osmic acid reducing bodies, that is neutral fats and fatty acids. Grossly, the mucosa is swollen, pink or velvety, and flecked over thickly with pin-point yellowish granules." The mesentery is very thick, feels like rubber, and may be very yellow.

The mesentery on microscopic examination reveals marked dilatation of lymphatic vessels filled with masses of fatty acid crystals. Mingled with the deposits of fatty acid crystals are polynuclear giant cells as well as large mononuclear cells of polyblastic type. The glands per se vary in appearance dependent upon the stage of reaction present. Following the invasion of the fat masses by the giant cells, one can see greater destruction of gland tissue with an invasion of fibroblasts and capillaries, resulting in ecchymosis. The giant cells and large mononuclear cells predominate even more and the fat deposits are likewise increased. This process was well described by Pearse[9] who stated, "The final stage shows a very large giant cell packed with fat deposits of all sizes and shapes and the stroma is made up of dense fibrous tissue full of ecchymoses and giant mononuclear cells."

The lipid chemistry in this disease is interesting. Whipple[1] found 80 per cent of the dry stool in his original case to be fat; 50 per cent was neutral fat and 30 per cent fatty acids. In the lymph nodes the ratio of fatty acids and neutral fat was 15 to 85. Apperly and Copley[11] found the same ratio to exist in their case. The total fatty acids, cholesterol and lecithin, are low in the fasting blood and are not increased by a test meal of cream and butter.

Necropsy findings in the various reported cases show a large incidence of fibrous pericarditis, seven cases being thus involved. The pancreas in most instances is normal, but has showed a moderate fibrosis in a few cases, though never sufficient to even be a suspicious causative factor. Chylous ascites has been found in four cases.

An exploratory laparotomy has been performed in eight cases, namely, by Whipple,[1] Apperly and Copley,[11] Amsterdam and Grayzel,[15] Pearse,[9] and three cases by Pemberton,[13] and in our case. The last case is the only one in which mesenteric thrombosis was present, and the only case in which it was necessary to resect the small intestine. Incidentally, the same intestinal lesions were found in the distal and proximal ends of the infarcted bowel specimen removed at operation as were found at autopsy in the remainder of the small intestine.

The etiology of intestinal lipodystrophy is most puzzling and several theories have been advanced. Sailer and McGann[10] stated, "The essence of the pathological process appears to be a local necrosis of fat tissue with liberation of lipolytic ferment from the damaged cells." The modus operandi of this necrosis and the nature of the ferment were not revealed. Rokitansky[17] described a condition in 1885, wherein there was a dilatation of the mesenteric lymph nodes with chyle. Jarcho[4] believed that dilatation of the lymphatics is the essential characteristic. The obstruction of the thoracic duct is not of much significance as an etiological factor, for such a finding has not occurred at autopsy. Again, Fairley and Mackie[18] have shown that there is no anatomic evidence of deposition of fat in lymph nodes of cases with thoracic duct obstruction. From the evidence at hand, one can surmise that there are no abnormal fats present in Whipple's disease, but that an excess of neutral fat and fatty acids is present in the mesentery, intestines, and stools. There is no excess of these lipids in the blood stream so it seems reasonable to explore two possible sources of explanation. The first is the possibility of failure by the organ to prepare the fat for absorption. Autopsies in these cases have failed to reveal any pancreatic insufficiency. Blumgart[2] has shown that the lipase content of the intestine is normal, and this further supports the contention that there is no fault of preparation. The remaining source of explanation involves several questions. Is the avenue of absorption into the blood stream at fault? This query appears to hold the answer, and was stressed by Ryle[19] and Apperly and Copley.[11] The following factors appear to show that there is a fault in absorption: (1) Despite the increased fat present in the intestine and mesentery, there are low cholesterol, lecithin, and total fatty acids in the fasting blood. Furthermore, a test meal of cream and butter does not in-

crease these values. Reinhart and Wilson[7] have shown that the dilated lymph channels and lymph nodes of the mesentery are rich in fat content as Whipple[1] originally stated. This also has been stressed by Jarcho[4] and Ryle.[19] These findings suggest another question, which is: "Why should the lymphatic lacteals be obstructed?" There is strong experimental evidence by Haas[20] to show that an acute inflammatory process in interstitial tissue can be aroused by the presence of unsaturated fatty acids with numerous eosinophils being present. Saturated fatty acids cause an inflammatory process with multinucleated giant cells, macrophages, and lymphocytes predominating. Thus, the inflammatory role played by lipids is a highly suggestive answer to the last possibility. There remains the question, "Why are these fatty acids in the lacteals?" Rinehart and Wilson[7] have attempted to answer this by theorizing that fats are reabsorbed from the intestine in increased amounts. Whipple's disease is a disturbance of the fat metabolism and does not appear to have much surgical significance other than in diagnosis. However, in the case herein reported the patient did die of peritonitis resulting from a mesenteric thrombosis. It is the first case of Whipple's disease that has had such a course. The only case reported as cured is that of Pearse.[9] His patient was placed on bile salts therapy and showed definite improvement with diminution of fat content of the stool. Pearse concluded that the cause of this disease was an abnormal absorption and utilization of fat. He is of the opinion that bile salts therapy corrects this and offers a working basis for the management of the disease. No one is in a position to confirm or deny this hypothesis and it offers the sole therapeutic measure at present.

TABLE I. ETIOLOGICAL THEORIES OF WHIPPLE'S DISEASE

AUTHOR	THEORY
Jarcho[4]	Deficiency of pancreatic lipase
Pearse[9]	Faulty bile duct metabolism
Apperly and Copley[11]	Failure of fat resynthesis with retention of fatty acids in tissue
Glynn and Rosenheim[21]	Possible adrenal factor
Hill[5]	Obstruction of thoracic duct and mesenteric lymphatics
Reinhart and Wilson[7]	Malabsorption of fat
Rosen and Rosen[14]	Possibility that Whipple's disease is not a clinical entity

CONCLUSION

The literature on Whipple's disease, a rare disease of fat metabolism involving the small intestine, has been reviewed. Another case has been reported with a most unusual complication, mesenteric thrombosis. The disease offers a problem in diagnosis and the only treatment offered thus far is bile salts therapy. From the maze of conflicting data, one can conclude that the multiplicity of theories concerning the etiology of Whipple's disease is sufficient evidence that the etiology is unknown. Whipple's disease should be considered as a possibility in cases of chronic fatty diarrheas.

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HUGE CHONDROSARCOMA OF RIB

Report of a Case

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A CASE of chondrosarcoma of the rib is presented because of its rarity in this location, because of the huge size which it attained, and because of the method employed in closure of the chest defect.

CASE REPORT

The patient was a white woman, aged 25 years, who complained of a mass under the left breast which had been enlarging for two years. This mass did not bother her until three weeks before admission to this hospital. During the last three weeks she had complained of shortness of breath, especially when she leaned forward. She had not previously consulted a doctor.

Eight years previously she had been in a car accident and injured the left side of the chest. At that time there was a moderate amount of pain along the ribs in the left anterior axillary line over the sixth rib, but there was no bruise or break in the overlying skin. A few months following the accident she noticed that a small hard mass measuring about ½ inch in diameter and height was attached to the sixth rib along the left anterior axillary line. This small mass along the rib started to enlarge two years before admission, and it grew steadily to its present huge size. She noticed no cough. Appetite and general condition were excellent.

On examination the patient was found to be well developed and well nourished. The breast was displaced anteriorly and medially by a large tumor mass which measured 20 by 25 cm. The tumor extended from the midaxillary line to within 3 cm. of the sternum, and it extended up to the fourth rib and down to the seventh rib (Fig. 1). The mass was as firm as the adjacent ribs, and seemed to be part of the ribs. It was nodular and there was limited motion between the tumor and the overlying skin. The chest appeared to have no mediastinal shift, and respirations were heard equally on both sides. The heart was normal. Blood pressure was 120/84.

Roentgenograms of the chest showed a very large soft tissue shadow on the anterior lateral portion of the left lower part of the chest. The central portion of this soft tissue mass contained a large amount of dense irregular calcific material (Fig. 2). A diagnosis of chondrosarcoma was made, and it was thought that the lesion had arisen from the lateral portion of the left sixth rib.

Since the tumor seemed well delimited, the decision was made to excise it. The anesthetic was intratracheal cyclopropane.

Two curved incisions were made from the head of the humerus to the costal margin, including an elliptical segment of skin 22 by 8 cm. The breast was also included, because at this time it could not be determined whether the tumor involved breast tissue. Skin and subcutaneous tissue were easily dissected from the tumor both medially and laterally.

It was found that the fifth, sixth, and seventh ribs were incorporated in the tumor. Thirty centimeters of these ribs were resected, going 2 cm. medially and 4 cm. laterally to the tumor. There was a layer of tumor between the pleura and the ribs 4 to 6 cm. in thickness. A block dissection was made, including ribs with attached tumor, muscles, soft tissues, and pleura. No adhesions between the lung and the tumor were noted. There was, however, a 5 mm. pearly white nodule on the surface of the lung near the lower margin of the upper lobe. This nodule was excised, including a little lung tissue about it.

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A 30 by 14 cm. defect in the chest wall was closed by a graft of fascia lata. Over this was placed a pedicle graft from the anterior portion of the latissimus dorsi muscle. The pedicle was left attached superiorly to preserve its nerve and blood supply. A Foley catheter was inserted into the pleural cavity through a stab wound below the incision. A Penrose drain was inserted between the muscle graft and the subcutaneous tissue. The skin was closed with continuous silk suture.

Pathologic Report (Mrs. S., Univ. Hosp. No. 93533).—The tumor mass measured 30 by 25 by 14 cm. and weighed 2940 Gm. One surface was covered by an elliptical segment of skin measuring 20 by 6 cm. This had a nipple and an areola near one margin. The underlying breast tissue was well defined from the underlying nodular mass and was normal in appearance.

Fig. 1.—Preoperative photograph showing the huge size of the chondrosarcoma involving the left fifth and sixth ribs.

The mass of firmer tissue was irregularly lobulated. The cut ends of three ribs protruded on opposite margins. Section across the mass showed pearly-white translucent tissue which centrally became more yellow, less firm, and somewhat more opaque. There were numerous small cavities ranging from 0.5 to 3 cm. in diameter. These cystic spaces were filled with a slightly yellow, clear viscid fluid. Centrally in the position of the middle member of the three ribs included was an irregularly shaped area of bone formation measuring 6 by 3½ by 5 cm. This bone contained red marrow. The upper of the three ribs showed slight irregularity of its periosteal surface; the lower rib was not involved in this tumor mass.

There was also a 5 mm. nodule of tissue which was solid and pearly-white embedded in lung parenchyma.

Microscopic.—The cartilage part of the tumor was highly cellular with large plump cells (Fig. 3). Multinucleated cells were common and multiple cells were present in many

lacunae. There was little evidence of regular orientation of cells (Fig. 4). Sections of the bony area showed a layer of fibrous tissue interposed between the bone and cartilage so that the two tissues were not intimately intermingled. Section of tumor made from the lung showed a highly cellular cartilage with considerable variation in size of cells and frequently more than one cell was present per lacuna. Multinucleated cells were not apparent. There is no apparent order in arrangement of cells.

Diagnosis.—The diagnosis was chondrosarcoma of the fifth and sixth ribs.

Fig. 2.—Roentgenograms of the chest showed a very large soft tissue shadow on the anterior lateral portion of the left lower chest. The central portion of this soft tissue mass contained a large amount of dense irregular calcific material.

Postoperative Course.—Postoperatively the patient was given oxygen intranasally, and penicillin intramuscularly. Continuous suction was applied to the catheter placed in the pleural cavity. She had a temperature reaching 101° F. for six days, and 100° F. for six more days. One hundred twenty cubic centimeters of serosanguineous fluid were aspirated from the pleural cavity on the fourth postoperative day. She had a surprisingly tranquil convalescence and complained more of pain in the thigh at the donor site of fascia lata than of discomfort of the chest.

Since the operation, the cardiac pulsation is very obvious in the medial part of the rib defect. There is a rather slight retraction on inspiration, but this retraction is not disturbing the patient.

To offer some protection to the rib defect, a kidney-shaped aluminum plate was designed and fitted to the curvature of the chest wall. She wears this for protection only when she may be in a crowd (Fig. 5).

Fig. 3.

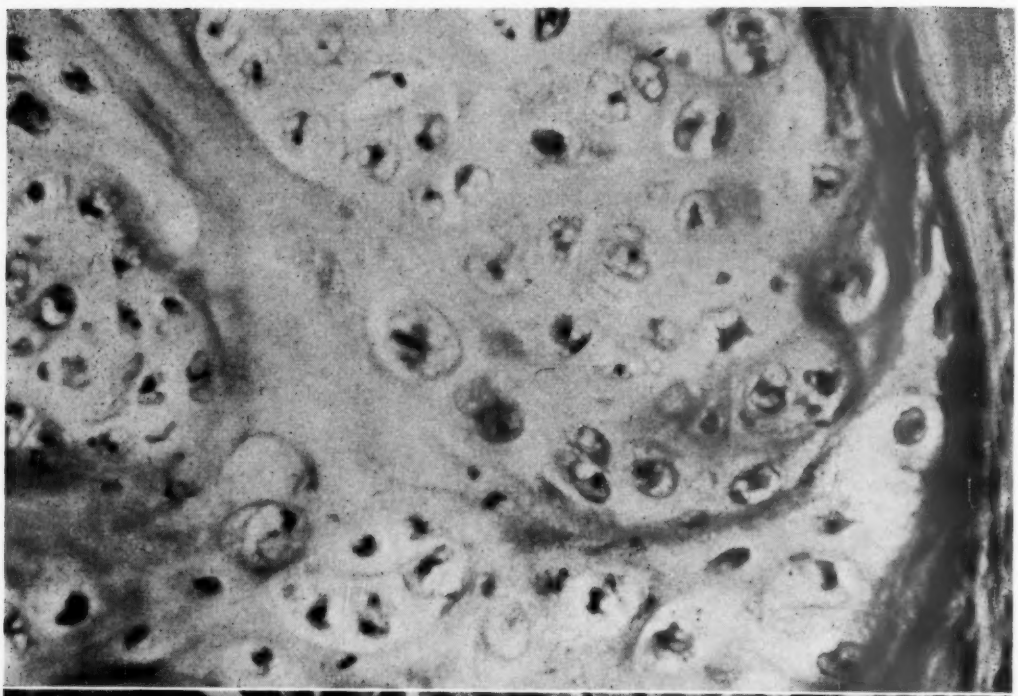

Fig. 4.

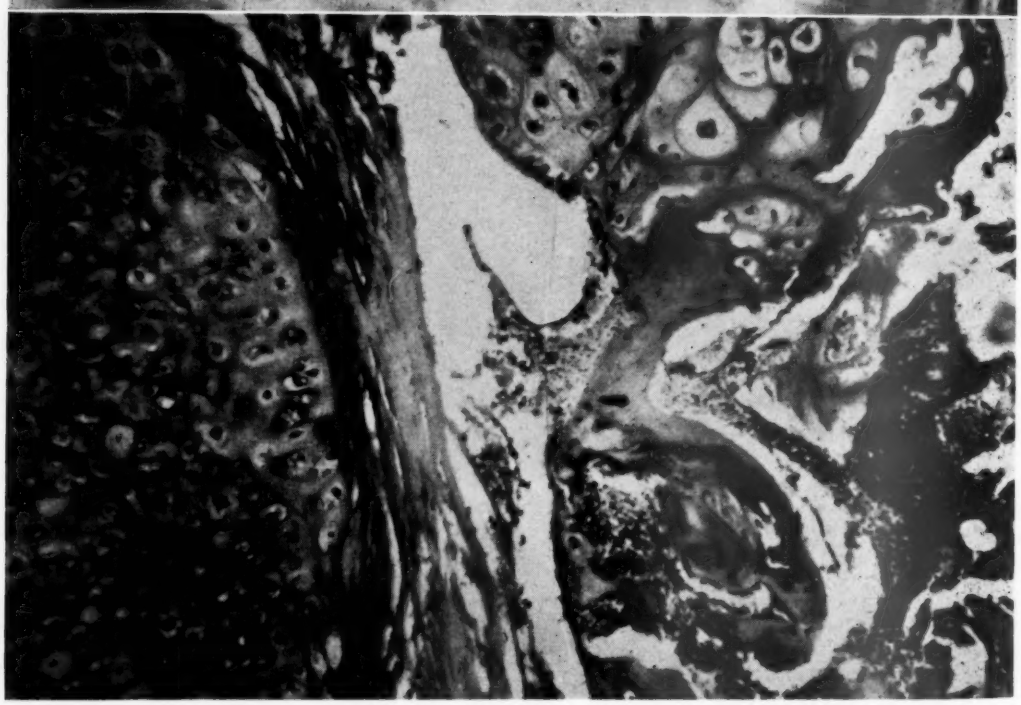

Fig. 3.—Photomicrograph, high power, showing that the cartilage part of tumor is highly cellular with large plump cells. Multinucleated cells are common and multiple cells are present in many lacunae.

Fig. 4.—Photomicrograph, medium power, of chondrosarcoma of rib showing little evidence of regular orientation of cells. In this section of the bony area there is a layer of fibrous tissue interposed between the bone and cartilage so that the two tissues are not intimately intermingled.

Since no apparent tumor remained, and because of the radioresistance of cartilagenous tumors, no deep roentgen therapy was given.

This patient was seen three months after operation, and there was no evidence of local recurrence. General health was excellent and she was able to carry on all her usual activities.

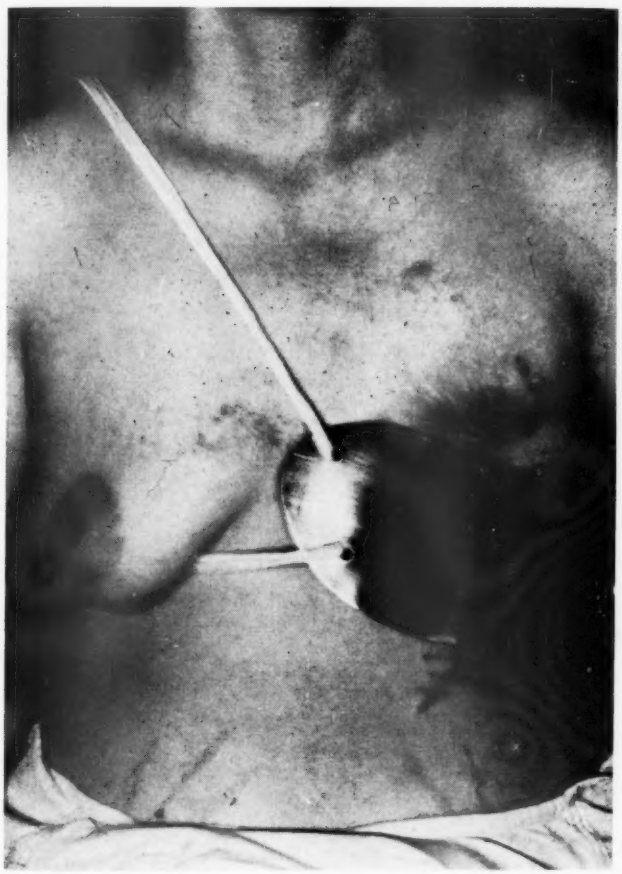

Fig. 5.—Postoperative photograph showing the location of the incision and the protecting metal shield.

DISCUSSION

Chondrosarcomas of the ribs that have been reported were usually small.[2-5] One other large tumor was presented by Harper.[1] This tumor followed trauma. It grew slowly for six years, then it enlarged greatly.

In Harper's case, and in this case, a small nodule was present for several years before rapid growth began. One can only speculate as to whether this represents disturbed healing of a rib fracture, or whether injury in the area called attention to a pre-existing nodule, perhaps an osteochondroma attached to the rib.

Since doing this operation, we find that Mayer[4] had also used fascia lata to close a similar operative defect. We have been unable to find any record of a case in which latissimus dorsi muscle was used as a pedicle graft to help close a defect in the chest wall. Firmness was obtained by the fascia lata and

increased protection, thickness, elasticity, and movability for the skin by the latissimus dorsi muscle graft.

CONCLUSIONS

1. A case of huge chondrosarcoma arising from the left sixth rib and extending to the fifth and seventh ribs has been presented.

2. There was a history of trauma followed by slow growth for six years, and then rapid growth to an enormous size in two years.

3. A large operative defect in the chest wall was repaired by fascia lata and a pedicle graft of latissimus dorsi muscle with excellent functional results.

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Editorial

The Quest for a "Blood" Substitute

DURING the last ten years much effort has been devoted to find the elixir that is epitomized by the term "blood substitute." By its very definition, a substitute should have all or many of the attributes of the material which it is to replace. A moment's reflection will prove that there is no substitute for blood. The term, "blood substitute," is a misnomer. It can denote only the particular properties that the individual defining the term may have in mind.

If we remove the attributes of the red blood cell and of the other formed elements from our considerations we are limiting our search to a material that can replace the known and suspected functions of plasma. These functions may be defined briefly as: (a) maintenance and stabilization of the blood (plasma) volume, (b) transport of hormones between tissues (c) transport and mobilization of antibodies, (d) protection against blood loss by components of the clotting mechanism, (e) transport of lipids and other substances closely associated with the plasma proteins, and (f) the nutritive functions of the plasma proteins.

A complete plasma substitute should attempt to fulfill the attributes just listed. Here again a moment's reflection will convince one that the only substitute for plasma would be plasma itself. From the practical and economic point of view the supply of this "natural" substitute cannot meet the potential needs for such a replacement solution.

Therefore, our definition must be further delimited to encompass those qualities that are needed to the greatest degree. What we are seeking predominantly is a material that, first, will maintain and stabilize the blood volume in those situations where this is of greatest importance and that, second, may have nutritive properties. It is too much to ask of any material that it also furnish hormones, antibodies, etc. Accordingly, our philosophers' stone should be sought in the name of a plasma colloid substitute.

What are the requirements that such a substance should have? Some of these may be listed: It should have an acceptable molecular size that will make it an active plasma colloid; it should be retained in the blood stream for a suitable period of time; it should be nontoxic, and not be deposited in the tissues. If excreted as such it should not cause nephrotoxic changes. It should be disposed of by the body by common metabolic pathways which would imply that its structural units and chemical linkages can be attacked and hydrolyzed by the enzymes of the tissues.

Let us consider some of the materials that have been proposed and investigated under the heading of "blood substitute," but more accurately defined as a plasma colloid. Gum acacia and pectins have been investigated. True, they do have the requisite colloid osmotic effect, but nature did not endow the

animal body with enzymes capable of hydrolyzing these pentosans. Consequently, they were found to be deposited in the tissues to a greater or lesser degree, with deleterious results. A material so foreign to our body economy does not fulfill the second major requirement, namely, that of being utilized. Polyvinyl pyrrolidine, polyvinyl alcohol, and methyl cellulose are also completely foreign to the body.

Two materials, dextran and gelatin, having colloidal osmotic activity have also been investigated. Both are composed of simpler units natural to the body. The former is composed of D-glucose, predominantly in 1:6 α glucoside linkage. It is derived from a bacterial polysaccharide which has been hydrolyzed to a molecular weight of around 100,000. The latter is a derived protein prepared from collagen by chemical treatment. It is composed of L-amino acids linked together by peptide bonds. Both its constituent amino acids and manner of linkage are entirely natural to the body. Both should furnish metabolizable energy if they are hydrolyzed completely within the body.

In a recent editorial in the *Journal of the American Medical Association* (**139**: 850, 1949), "Dextran as a Plasma Substitute," a comparison is made of Dextran, the plasma proteins and gelatin. It is with these comparisons that a further word of clarification is necessary. Distinctions are drawn which are not as clear-cut as they are reported to be. Neither Dextran nor gelatin has the globar form in their molecular dimensions which is found in serum albumin. This disparity of molecular parameters has much to do with the fact that approximately 25 per cent of Dextran and 50 per cent of gelatin injected intravenously are excreted through the kidneys in their original form. Both substances must be partially hydrolyzed by chemical means before they are useful as plasma colloid substitutes. This reduction in molecular size which is thereby achieved increases the osmotic activity of the preparations and reduces the likelihood of pathologic storage of the original macromolecules. Both of these substances are composed of substances entirely native to the body and nothing so far reported significantly demonstrates the superior value of Dextran over gelatin in this regard.

There has been far too much loose talk and poor writing on this subject. The factors which will determine the relative value of these two substitutes will reside in other physical attributes of the materials, their relative ease of preparation, and the safety of their parenteral administration.

—*I. S. Ravdin.*

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

EXPERIMENTAL EMBOLISM OF THE PULMONARY ARTERIOLES AND CAPILLARIES

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THERE have been numerous investigations concerning the mechanism of death in pulmonary embolism. Likewise, there have been many attempts to reproduce in animals the different types of pulmonary embolism seen in human patients. Churchill[1] classified the types of fatal pulmonary emboli as: (1) complete obstruction with immediate death; (2) partial obstruction with delayed death, which he attributed to reduced effective blood volume, causing a diminished cardiac output with falling blood pressure and rising venous pressure; and (3) partial obstruction with delayed death, in which there was a component of failure of the right side of the heart. Katz[2] classified pulmonary emboli into (1) the large snakelike embolus which rides the bifurcation or plugs either main branch of the pulmonary artery, (2) the emboli of intermediate size which occur in showers and plug smaller pulmonary arteries, and (3) the more minute emboli occurring in showers which plug the arterioles. This last classification reflects the methods used by various investigators, for a partial survey of the field shows that emboli have been produced in: (1) the pulmonary artery or either of its main branches,[3-12, 22] (2) the smaller pulmonary arteries,[10, 11, 13-17, 22] or (3) the arterioles and capillaries.[3, 11, 14, 17-23]

Emboli of the last type, that of the arterioles and capillaries, have excited much interest because of the apparent disproportion between the amount of lung tissue affected and the symptoms produced. This has resulted in the use of suspensions of starch or barium sulfate as agents in attempts to reproduce this phenomena in animals.

HISTORICAL REVIEW

As far as can be determined from the literature, Dunn[20] was the first in this country to use starch in experimental pulmonary embolism. He found that injecting 40 to 75 c.c. of a 1:4 potato starch suspension into the jugular vein or right ventricle of goats weighing 16 to 19 kilograms caused a great rise in venous pressure, a fall in systemic blood pressure, and death in five to thirty minutes, with respiratory failure occurring before the heart stopped beating. Microscopic examination of the lungs of these animals showed all pulmonary arterioles up to 2 mm. in diameter filled with starch granules. He did not mention the size of these granules.

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In a second series of goats he found that lesser doses of the starch suspension produced death in one to eight hours, there being a gradual downward progression during this period. Dunn showed that in this type of pulmonary embolic death there is a normal percentage of saturation with oxygen of the arterial and venous systems after embolization and also that the carbon dioxide content in arterial blood was essentially unchanged by embolism. He found that the tachypnea induced by moderate doses could be prevented or eliminated by bilateral cervical vagotomy. His conclusion was that the tachypnea was caused by spasm of the bronchial musculature. Regrettably he did not state what influence, if any, the vagotomy had on the lethal effect of the emboli. It is important to note that he did not find starch granules in the cerebral or renal vessels and expressed the belief that his experimental findings were not the result of the presence of starch in organs other than the lungs.

Binger, Brow, and Branch[19] repeated the procedures of Dunn, using in dogs a 1:20 suspension of potato starch in saline solution. They also showed the influence of the vagi on the tachypnea when they prevented or eliminated it by freezing both vagi and went further to show that the tachypnea of an oxygen want or of a carbon dioxide excess was similarly affected by freezing both vagi.

The starch granules used in their experiments ranged from 5 to 60 microns, averaging 20 to 40 microns. They reported that starch could not be found in any organ except the lungs, and that in the lungs it was lodged in the arterioles and capillaries of all lobes, being predominantly in the arterioles. They suggested that the effect of starch is not of an irritative nature as shown by results of the gradual infusion of the starch suspension into an animal. An effect was not seen until a certain amount of starch had been given and then the effect was dramatic.

Villaret, Justin-Besançon, and Bardin[23] noted that sectioning the vagi of rabbits increased seven times the amount of powdered pumice stone necessary to produce sudden death. After sectioning the cervicothoracic sympathetics they reported that one-fourth of the previously fatal amount injected was lethal. They also showed that epinephrine and atropine in combination could delay sudden death. These workers suggested that sudden death was due in part to reflex sympathetic inhibition. Shock was considered by them to be the manifestation of the inhibition.

De Takats, Beck, and Fenn[3] injected an 8:17 suspension of potato starch in water into the ear veins of thirty-five rabbits and found that 2 c.c. was the minimal lethal dose, causing dyspnea, cyanosis, convulsions, and death in every animal in five minutes. One and one-half cubic centimeters of the suspension killed 30 per cent of the animals injected; 1 c.c. killed none. Sublethal doses were found to cause dyspnea, cyanosis, restlessness, micturition, and defecation but within one-half hour the respiration, pulse, and color of the animals were normal. Microscopic examination of the lungs showed the starch granules, ranging from 50 to 150 microns in size, in the lobular arteries,

arterioles, and walls of the alveoli. They did not report examining the heart or brain microscopically. In these experiments an anticoagulant was not used.

These authors concluded that pulmonary hypertension proximal to an obstructing pulmonary embolus is the essential cause of death and is responsible for the electrocardiographic changes. It is their opinion that the pulmonary vasoreceptors, both vagal and sympathetic, are highly sensitive and that they are capable of producing such widespread changes as vasoconstriction in the pulmonary vascular bed, a fall in blood pressure, vagal inhibition of the heart, coronary constriction, and bronchial spasm. Thus, they feel that certain neurocirculatory changes are the major contributory causes of death in smaller pulmonary emboli which, by virtue of the minor amount of pulmonary tissue devitalized, should not cause death.

Jesser and de Takats[24] reported that vagal mediated reflex bronchoconstriction and bronchosecretion were induced experimentally by pulmonary embolism and that in human beings these responses are some of the major causes of postoperative pulmonary atelectasis.

Megibow, Katz, and Steinitz[22] studied the three forms of emboli, using the massive emboli method of Mendlowitz[12] and using pea seeds for embolization of smaller arteries and a 1:20 starch suspension for embolization of the arterioles and capillaries, after the method of Binger, Brow, and Branch.[19] They found in their studies of starch embolization of dogs that the elevation of pulmonary arterial pressure could be integrated with increased pulmonary arteriolar resistance resulting from the mechanical obstruction by the starch granules in the arterioles, since repeated dosage of the suspension produced further increments of pressure elevation. They expressed the belief that the cause of death is the embolus in the pulmonary arterial tree, acting as a direct mechanical deterrent to the flow of blood through the lungs.

Megibow, Katz, and Feinstein[11] studied the kinetics of respiration in pulmonary embolism, using a 1:20 suspension of starch in dogs. They showed in experiments with massive emboli that distention of the great veins, particularly the mouth of the superior vena cava, by pulmonary hypertension caused tachypnea and dyspnea, which in turn could be eliminated by bilateral cervical vagotomy. In embolization with starch they postulated that the cause of the tachypnea was a reflex arising from distention of the smaller pulmonary arteries by starch and they explained the absence of dyspnea in this type of embolism by suggesting that this reflex overpowered that arising from distention of the great veins. Bilateral cervical vagotomy in these experiments decreased but did not eliminate the tachypnea. They did not use heparin in their experiments and microscopic examination showed antemortem clots around the starch granules.

Kinney, Haynes, and Dexter[15] described a new method of producing pulmonary embolism. A Cournand catheter was introduced into the external jugular vein and passed under roentgenoscopy to either branch or a smaller ramification of the pulmonary artery. Haynes, Kinney, Hellems, and Dexter[14] placed a balloon on the end of a venous catheter which was inserted into a

lobar pulmonary artery. The balloon was then dilated by a pressure higher than that in the pulmonary artery so as to obstruct the blood flow to that lobe. The obstruction and distention of the lobar pulmonary artery in this manner did not produce a constant change in the respiratory rate, pressure in the femoral and pulmonary arteries, or heart rate of anesthetized and unanesthetized dogs. In contrast, they stated, precapillary emboli produced by the slow infusion of a 1 per cent suspension of Lycopodium spores measuring 25 to 30 microns in diameter into a lobar pulmonary artery in anesthetized animals regularly produced an increase in respiratory rate, pulmonary arterial and right ventricular pressure, electrocardiographic changes, and a decrease in femoral arterial pressure, leading to death if the infusion was continued. There was a progressive fall in the cardiac output and only terminally was there a significant rise in peripheral venous pressure. The circulatory changes accompanying embolism were not abolished by vagus section and pithing of the spinal cord.

Binet and Burstein[18] reported using a suspension of Lycopodium powder in petroleum oil or barium sulfate in water as pulmonary embolic agents in dogs. They concluded that the hypertension of the lesser circulation is caused by a local reflex spasm of the pulmonary arterioles initiated by mechanical endovascular irritation by the embolizing particles and some peripheral reflex by excitation of the vagus, as well as the mechanical obstruction of the pulmonary arterial tree. Conversely, they concluded that the hypotension of the greater circulation is not a reflex but results from the mechanical obstruction of the blood in the lungs, which prevents its return to the systemic arterial tree. They felt that the mechanical obstruction of the pulmonary circulation by the emboli was insufficient to explain the pressure changes which occurred in the pulmonary artery. In their opinion, this could be explained by an intense spasm of the pulmonary arterioles in addition to the mechanical obstruction. They found that during the embolism a peripheral vasoconstriction existed because of the diminution in the cardiac output.

Smith and Hara[17] in a recent preliminary report stated that in anesthetized heparinized dogs with open thoraces fine urethral or ureteral catheters were introduced into the right ventricle or the main pulmonary artery through a small stab incision and guided to any lobar arterial branch. Suspensions of starch or barium sulfate, both found equally effective, were then introduced into the artery in selected doses in such a way as to prevent retrograde flow of the material. The dogs died two to three minutes after the injection. However, when such agents as fine glass beads, poppy seeds, or Lycopodium spores were injected there were no significant effects. Since embolic particles such as beads or Lycopodium spores did not produce circulatory dynamic changes and finer materials produced severe circulatory changes, they reasoned that pulmonary "capillary" emboli, affecting a restricted portion of the pulmonary vascular bed, may cause death, apparently from pulmonary vasospasm and circulatory failure.

Because of the equal effectiveness of starch or barium sulfate in their experiments, they preferred to use barium sulfate most often, in a 5:4 sus-

pension, because of the ease with which it was injected as compared to a 1:1 starch suspension. In dogs weighing 10 to 15 kilograms, 2 to 3 c.c. was the usual dose injected slowly over a period of twenty to thirty seconds. Occasionally a ¼ inch (about 0.6 cm.) Penrose drain tubing or a wide rubber band was placed around the artery containing the catheter. In such instances the lethal effect was obtained after injection of the embolic material only by releasing the ligature.

Holden, Shaw, Cameron, Shea, and Davis[8] reported not finding any evidence to support the supposition that pulmonopulmonary, pulmonocoronary, or pulmonovagal depressor reflexes contribute to the death of dogs after massive pulmonary embolism. Cervical vagotomy was performed on eight dogs and resection of the stellate and upper four thoracic ganglia, as well as vagotomy, was done on four dogs. Changes in hemodynamics were consistent and precisely what were encountered in the control experiments. No more emboli were required to produce death than in the control series.

EXPERIMENTAL PROCEDURES AND RESULTS

In all experiments in which starch was the embolic agent a 1:2 suspension of cornstarch U.S.P. in saline solution was used. When barium was the embolic material, insoluble barium sulfate U.S.P. in a 1:1 suspension was employed unless otherwise stated. The starch granules were round or polygonal and ranged from 10 to 30 microns in diameter, averaging about 18 microns. The barium sulfate particles were the same shape but were generally larger, averaging about 25 microns in diameter. Unless indicated to the contrary, every animal was heparinized. Pentobarbital sodium and chloralosane were the anesthetic agents.

Embolism With Starch in Rabbits and Dogs.—Rabbits weighing 2 to 4 kilograms were used. They were heparinized and five minutes later the starch suspension was injected into an ear vein. This was followed by 1 c.c of saline solution. The animal was then freed and observed.

Those that died showed the symptoms described by de Takats, Beck, and Fenn[3]; namely, dyspnea, cyanosis, and convulsions resulting in death in five minutes. The minimal lethal dose was found to be 1.5 c.c. of the suspension (Table I). Sublethal doses in the higher levels occasionally caused lethargy, dyspnea, or possibly cyanosis and death. Most often there was not an effect from a sublethal dose.

The heart, lungs, and brain of one animal from each group in Table I were examined microscopically for identification of the starch granules in these organs. In the lungs the starch granules were found scattered diffusely throughout the pulmonary arterial tree and lodged in great numbers in the capillaries. Occasionally a few were seen in arterioles. The arterioles were

TABLE I. RESULTS OF INJECTING 1:2 SUSPENSION OF CORNSTARCH U.S.P. INTO EAR VEIN OF HEPARINIZED RABBITS

RESULTS	0.25 c.c.	0.5 c.c.	1.0 c.c.	1.5 c.c.	2.0 c.c.
Died in five minutes or less		2	1	5	5
Did not die	5	3	4	.	

usually greatly dilated. It was observed that the quantity of starch granules found in the lungs was increased in direct proportion to an increase in the amount of starch suspension administered to the rabbits. Occasionally the starch granules could be found in the heart, lodged in the capillaries, but they were found in very small numbers only after long, diligent search. Even more rarely, lesser numbers could be found in the capillaries of the brain after extensive examination. It is questionable whether the number of starch granules found occluding the capillaries of the heart and the brain of these rabbits was sufficient to have produced death.

Prinzmetal and associates[16] have shown that there are pulmonary arteriovenous anastomoses in anesthetized rabbits, cats, and dogs. They proved this by the injection of glass spheres suspended in saline solution into the right ventricle or pulmonary artery of the experimental animal and the demonstration that they could be recovered in the pulmonary veins and liver. The maximal size bead recovered varied from 160 to 290 microns in rabbits and 100 to 180 microns in dogs and measured 390 microns in one cat.

Nine dogs were used to determine the minimal lethal dose of the starch suspension when injected into a jugular vein or the right atrium. In each case the dog was anesthetized with pentobarbital sodium, the thorax was unopened, and the animal was heparinized. Simultaneous measurements of the carotid and right atrial pressures were recorded, using a No. 10 French polyvinyl catheter, a water manometer for the latter and a mercury manometer for the former. When the starch suspension was injected into the right auricle, the No. 10 French, polyvinyl catheter recording its pressure was used. The starch was injected in graded doses proportionate to the kilogram weight of the dogs.

It was found that 0.5 c.c. of the suspension of starch per kilogram weight of the dog was the minimal lethal dose. This dose caused dyspnea, a sudden precipitous fall in systemic blood pressure to 20 or 30 mm. of mercury, and an average rise of 15 cm. of water in the right atrial pressure with death in two to five minutes in five dogs. Those animals given a sublethal dose of the suspension of starch had a drop in the carotid blood pressure of 30 to 50 mm. of mercury, from which they recovered in less than one minute. In one animal there was another fall in the carotid pressure several minutes after the first, but the animal recovered. The right atrial pressure occasionally was altered, showing a slight but never sustained rise in pressure. Dyspnea was seen in these animals only during this period. In those animals that died, necropsy showed extreme dilatation of the right side of the heart with thrombi absent from the heart or lungs. Probably because of the scattering of the starch suspension throughout all lobes of the lungs, the starch could not be found grossly in the pulmonary arterial system. Four animals given sublethal doses were apparently unaffected and were killed one hour after the injection. These dogs were found to be normal with no evidence of dilatation of the right side of the heart, thrombi, or starch, except in one case, in which moderate dilatation was seen. It was realized that the dogs killed at the end

of one hour might have died later from the injections of starch but that period of survival was arbitrarily chosen.

To determine the influence of artificial insufflation of the lungs on the minimal lethal dose of the starch suspension, two dogs were anesthetized with pentobarbital sodium and their thoraces were opened on the midline, their lungs being artificially inflated. The carotid and right atrial or right ventricular pressures were recorded with mercury manometers and the dogs were heparinized.

When a minimal lethal dose of the starch suspension was injected into the right atrium of one of the animals its blood pressure fell from 107 to 50 mm. of mercury in one minute and during the next five minutes the pressure rose to 80 mm. From this point the carotid pressure gradually fell, the right atrial pressure rose, and the dog died thirty minutes after the injection. Necropsy showed the same findings as in the control series. The other animal, when the minimal lethal dose of starch was injected, had a sudden fall of carotid blood pressure from 110 to 30 mm. Then the pressure rose to 80 mm. In this animal the right ventricular pressure was recorded; it rose from 6 to 22 mm. of mercury when the injection was made and it held this level until several minutes before the animal died, when it gradually fell to 2 mm. The carotid pressure gradually fell from 80 mm. to 0 in fifty-five minutes, at which time the animal died. At necropsy the right side of the heart was moderately dilated but not distended with blood. Thrombi or starch could not be found in the heart or lungs.

Three dogs were used to determine the influence of bilateral cervicothoracic sympathectomy and cervical vagotomy in animals with open thorax on the minimal lethal dose of the starch suspension. They were anesthetized with pentobarbital sodium and the thorax was opened on the midline. Bilateral sympathectomy was done from the stellate ganglion to the fifth thoracic ganglion and then a bilateral cervical vagotomy was performed. The animals were heparinized, after which a minimal lethal dose of the starch suspension was injected into the right atrium.

One animal died in three minutes after symptoms seen in the control series. The second animal had a fall in carotid pressure of 70 mm. of mercury but in one minute the pressure had returned to normal. Bigeminal cardiac rhythm then developed and lasted until the animal was accidentally killed at the end of thirty minutes. At necropsy it was found that the heart was moderately dilated on the right side and distended with blood. However, thrombi or starch particles could not be found in the heart chambers or pulmonary arterial system. The third animal showed a response similar to that of the second dog. The carotid blood pressure fell 60 mm. of mercury and returned to normal in one minute. Trigeminal cardiac rhythm then developed and the dog died in fifteen minutes. Necropsy findings were the same as in the second dog.

The influence of bilateral cervicothoracic sympathectomy and cervical vagotomy with closed thoraces was determined in a series of three dogs. Bilateral sympathectomy was done from the stellate ganglion to the fifth thoracic

ganglion through the third intercostal space on each side and the thorax was closed. Then the procedure was continued as on the foregoing three dogs. These animals died in two minutes or less after the injection. The necropsy findings were the same as those in the control series.

Embolism With Barium Sulfate in Dogs.—Stimulated by the work of Smith and Hara,[17] we performed the following experiments. Nine dogs weighing 7 to 23 kilograms were used (Table II). They were anesthetized and the thorax was opened on the midline. The carotid pressure was recorded in all experiments as a criterion of the animal's condition. A No. 9 French Cournand catheter was inserted into an external jugular vein and guided to a particular lobar artery according to the method of Kinney, Haynes, and Dexter.[15] If the animal was to be heparinized it was done at this point. Then the 1:1 barium sulfate suspension was injected into the Cournand catheter and washed in with 2 c.c. of saline solution, the approximate capacity of the catheter. The injection was made quickly and forcefully in all dogs. Depending on the size of the dogs, 2 to 8 c.c. of the suspension was injected. In three dogs 0.5 c.c. per kilogram of body weight was injected into the respective arteries. In some experiments the catheter was left in place and in others it was removed immediately after the injection, to be reinserted if desired. Neither of these conditions seemed to influence the results. If the animal did not die within thirty minutes of the injection, a pulmonary artery to another lobe was usually injected, preferably on the side opposite to the previous injection, and in two experiments a third injection was done.

If death did not result thirty minutes after a desired number of injections, the animal was killed and the heart and lungs were removed en masse. Any roentgenograms desired were taken at this point before the heart and pulmonary vessels were opened, thus avoiding disturbance of the anatomic and pathologic features. Then a careful examination of the heart was performed. Search was made particularly for thrombus formation, barium sulfate particles, and dilatation of the right side of the heart. We dissected the pulmonary artery and its branches as far as the smallest vessels, again attempting to find thrombi and barium sulfate particles. To determine whether the anesthesia was an important factor in the results, in four animals the anesthetic agent used was chloralosane, which does not sedate the nervous system as much as pentobarbital sodium. Heparin was used in only six of the nine animals.

Because Smith and Hara[17] sometimes used a temporary constricting ligature about the artery proximal to the injection, we employed their technique when administering the first injection to one animal.

Three of the nine animals died in two to seven minutes after the second injection of a lobar artery. In two of the three animals that died, heparin was not used and their deaths, both of which occurred in two minutes, probably can be attributed to this fact, for massive thrombi were found in the right auricles and ventricles of the hearts and in the pulmonary arteries. Death could conceivably have resulted from these thrombi. In one of these dogs the

TABLE II. EFFECT OF INJECTION OF A 1:1 SUSPENSION OF INSOLUBLE BARIUM SULFATE INTO SELECTED LOBAR PULMONARY ARTERIES OF ANESTHETIZED DOGS WITH OPEN THORACES. THERE WAS A 30 MINUTE LAPSE BETWEEN INJECTIONS

DOG	WT. (KG.)	ANESTHETIC AGENT	HEPARIN	AMOUNT OF BARIUM SULFATE AND SITE OF ARTERY INJECTED*	RESULT	POSTMORTEM FINDINGS	ROENTGENOGRAMS
1	12.5	Pentobarbital sodium	Yes	2 c.c. RUL	None	Right heart dilated and no clots in heart or vessels	None
				5 c.c. LUL	Died in 7 min.		
2	15.6	Pentobarbital sodium	Yes	3 c.c. LUL	None	Animal killed; no pathologic findings noted	Good localization of barium sulfate; none seen in the heart
				3 c.c. RLL	None		
				4 c.c. LLL	None		
3	23.0	Pentobarbital sodium	Yes	6 c.c. RML†	None	Animal killed; no pathologic findings noted	Good localization of barium sulfate; none seen in the heart
				6 c.c. LUL	None		
				8 c.c. RLL	None		
4	12.0	Pentobarbital sodium	Yes	4 c.c. RML	None	Animal killed; no pathologic findings noted	None
5	12.5	Pentobarbital sodium	No	5 c.c. LLL	None	Animal killed; no pathologic findings noted	Good localization of barium sulfate; none seen in the heart
6	7.6	Chloralosane	No	3 c.c. LLL	None	Right heart dilated; massive thrombi in right auricle, ventricle, and pulmonary artery	X-ray shows poor localization of barium sulfate; seen in all lobes; none seen in the heart
				3 c.c. RLL	Died in 2 min.		
7	12.8	Chloralosane	No	6.3 c.c. RLL	None	Right heart dilated; massive thrombi containing barium sulfate in right auricle and ventricle	X-ray shows barium sulfate in right heart, well localized in lungs
				6.5 c.c. LLL	Died in 2 min.		
8	16.0	Chloralosane	Yes	8 c.c. RLL	None	Animal killed; no pathologic findings noted	Good localization of barium sulfate; none seen in the heart
				8 c.c. LLL	None		
9	14.0	Chloralosane	Yes	7 c.c. LLL	None	Animal killed; no pathologic findings noted	Good localization of barium sulfate; none seen in the heart
				7 c.c. RLL	None		

*RUL, right upper lobe; LUL, left upper lobe; RLL, right lower lobe; LLL, left lower lobe; RML, right middle lobe.
†In this injection a constricting ligature was placed temporarily around the artery proximal to the injection and released after injection was completed.

roentgenogram revealed barium sulfate scattered throughout all lobes of the lungs, and in the other animal barium was seen in large amounts in the thrombi found in the heart and pulmonary artery. Evidently in these experiments there was a retrograde passage of the barium into the heart and death resulted. When the second lobar artery was injected in the third dog that died, its carotid pressure fell precipitously, the animal became tachypneic and died in seven minutes, with extreme dilatation of the right side of the heart. No thrombi or barium particles were present in the heart or pulmonary artery, and barium could be found only in the two lobar arteries injected. Whether there was a retrograde passage of the suspension with scattering into other lobes was not determined by roentgenogram. The possibility that this was the cause of death must be considered.

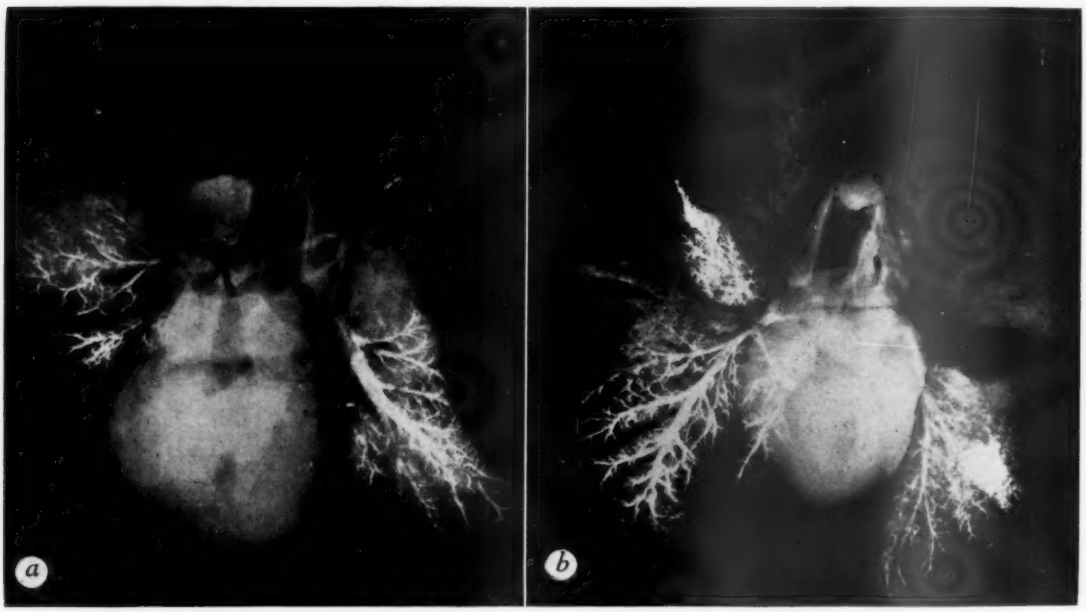

Fig. 1.—Roentgenograms of (*a*) Dog 2 and (*b*) Dog 3 showing localization of barium sulfate in selected lobar pulmonary arteries.

In the remaining six dogs, one of which was not heparinized, there were no significant effects from injection of insoluble barium sulfate suspension into one, two, or three lobar arteries. Occasionally there would be a slight momentary decrease in the carotid blood pressure or an increased carotid excursion after an injection, but beyond this nothing significant occurred. In five of the six dogs, roentgenograms showed the barium sulfate in the injected arteries without scattering into other lobes (Fig. 1). After these dogs were killed, by stopping the artificial insufflation of the lungs, necropsy did not reveal pathologic findings. A difference in response that could be attributed to a change in the anesthetic agent from pentobarbital sodium to chloralosane was not noted.

Thus, using the Smith and Hara[17] method in six dogs we were able to cause death in only one and in that case there remains the possibility that the dog died from multiple small emboli resulting from scattering of the barium sulfate throughout all lobes of the lungs. In three other dogs heparin was omitted and two of the animals probably died as a result of this omission.

In another series of experiments the foregoing technique was altered only as follows: six dogs, anesthetized with pentobarbital sodium and heparinized, were injected with a 5:4 suspension of barium sulfate (Table III). In five of them only the right lower lobar pulmonary artery was injected and the amount and rate were 3 c.c. in thirty seconds. The Cournand catheter used was of 2 c.c. capacity, so 5 c.c. was injected in fifty seconds to accomplish the foregoing result and to avoid the necessity to wash in the barium sulfate with saline solution, because this might cause a scattering of the embolic material into the other lobes of the lungs. After the injections the catheter was left in the injection position for the one hour control period, at the end of which time the animal was killed by stopping the artificial insufflation of the lungs if death had not already occurred. In the case of the sixth animal two injections consisting of 2 c.c. of the suspension were administered one-half hour apart at the rate of 1 c.c. per minute to the right middle lobar and left lower lobar pulmonary arteries, respectively. During each injection a

TABLE III. THE EFFECT OF INJECTION OF A 5:4 SUSPENSION OF INSOLUBLE BARIUM SULFATE INTO SELECTED LOBAR PULMONARY ARTERIES OF HEPARINIZED, ANESTHETIZED DOGS WITH OPEN THORACES

DOG	WT. (KG.)	AMOUNT, RATE, AND SITE OF BARIUM SULFATE INJECTION	RESULT	POST-MORTEM FINDINGS
10	6.8		30 mm. of mercury fall in carotid pressure, 3 mm. rise in right ventricular pressure; animal survived one hour, then killed	
11	8.8		40 mm. fall in carotid pressure and 4 mm. rise in right ventricular pressure; animal survived one hour, then killed	
12	16.6	3 c.c. barium sulfate into RLL artery in 30 seconds	36 mm. fall in carotid pressure and 4 mm. rise in right ventricular pressure; animal survived one hour, then killed	No pathologic features noted
13	22.0		42 mm. fall in carotid pressure and 4 mm. rise in right ventricular pressure; animal survived one hour, then killed	
14	9.3		Carotid pressure gradually fell to zero and right ventricular pressure gradually rose 10 mm. in 55 min., when dog died	Moderate right heart dilatation but no thrombi seen; no barium sulfate in left lung on microscopy
15	7.0	2 c.c. RML artery in 2 min.*	None	No pathologic features noted
		2 c.c. LLL artery in 2 min.*	None	

*In these injections a constricting ligature was placed temporarily around the artery proximal to the injection and released after each injection was completed.

constricting ligature was placed temporarily around the artery proximal to the injection and was released after each injection was completed.

Of the first five dogs, one died in fifty-five minutes. They all showed within a few minutes a fall in the mean carotid arterial pressure of approximately 40 mm. of mercury but in four dogs this level was maintained to the conclusion of the experiment. Simultaneously the mean right ventricular pressures rose 3 to 4 mm. of mercury and were maintained. In the one animal that died, the mean carotid arterial pressure continued to fall gradually to 0 in fifty-five minutes and the mean right ventricular pressure had risen 10 mm. of mercury above normal by the time death occurred. The sixth dog showed no response to the two injections. At necropsy pathologic features were not noted in any dog except the one that died. It exhibited moderate distention of the right side of the heart but no thrombi were seen. Barium sulfate could be seen grossly in the right lower lobar pulmonary artery. Roentgenograms were not taken in this series but microscopic examination of the left lung of the animal that died did not show that the embolic material had been scattered to the lung opposite to that injected.

COMMENT

In attempting to reproduce in animals the pulmonary embolic death seen in man from a disproportionately small blood clot, experimental investigators have turned to the use of starch and barium sulfate as embolic agents. In explaining the mechanisms of death in both animals and man, the investigators have divided into two schools of thought. The first postulates as the primary factor a nervous influence such as a vagal pulmonopulmonary or a pulmonocoronary reflex. The second group states that the mechanical factor of obstruction of the pulmonary arterial system is the primary cause of death and that neurogenic factors play a negligible role, if any.

The experiments of Megibow, Katz, and Steinitz[22] demonstrate the result if a minimal obstruction of the pulmonary venous return is created. They injected smaller amounts of starch granules into the pulmonary arterioles and capillaries than were used in our experiments. In one-half of their animals, they injected the starch suspension in divided doses. They noted that the elevation in the systemic venous pressure associated with a normal systemic arterial pressure persisted in some animals until death. This demonstrated the result of an obstruction of the pulmonary arterial system sufficient to place an increased load on the right side of the heart without reducing the cardiac output, causing gradual failure of the right ventricle. In other animals in spite of an elevated pulmonary arterial pressure both the systemic arterial and the venous pressures tended to decrease, reaching shock level in some instances just before the animals died. This showed the result of an obstruction of the pulmonary arterial tree sufficient to reduce the cardiac output in addition to placing an increased load on the right side of the heart, resulting in a reduction in the volume of blood circulating in the peripheral vascular tree, leading to a peripheral vascular collapse.

In our experiments a more complete and dramatic obstruction was achieved, resulting in an immediate, almost complete diminution of the cardiac output, relative coronary insufficiency, myocardial ischemia, and death. In the control group the animals given the "minimal lethal dose" demonstrated simultaneously a rise in right atrial pressure of 15 cm. of water and a precipitous drop in carotid arterial pressure to 20 or 30 mm. of mercury with death in two to five minutes. When the sympathetic chain from the stellate ganglion to the fifth thoracic ganglion was sectioned bilaterally and subsequently a bilateral cervical vagotomy was performed prior to the injection of a "minimal lethal dose" of the starch suspension, little alteration in the results from those found in the control group was noted. Thus, we were unable to note the influence of any neurogenic factors in the death of the animals given this dosage of a starch suspension.

In another study related to the neurogenic hypothesis of death from pulmonary embolization by particulate matter, an attempt was made to reproduce in twelve dogs the work of Smith and Hara[17] using a barium sulfate suspension. In only two dogs was death produced, in spite of the fact that two or three lobar arteries were injected in some animals. An intense vasospasm, the response to stimulation of neuroreceptors in the walls of pulmonary vascular system by the embolic material is considered by some authors, including Smith and Hara, to be the cause of death in embolism of the pulmonary arterioles and capillaries. This is further suggested by the work of Haynes, Kinney, Hellems, and Dexter.[14] It is believed by some that these stimuli elicit a massive reflex vasospasm of the pulmonary vascular bed and that death is caused by this reflex vasospasm, not by the simple mechanical obstruction of the arterioles and capillaries. In our first series of injections of a selected lobar artery, care was taken in the injection of the embolic material to exert as much pressure as was possible within the artery. Significant responses were not elicited by these forceful injections except in one animal and in that animal it is probable that the force of the injection succeeded only in causing a retrograde scattering of the embolic material throughout the lungs.

Furthermore, as was previously mentioned, Haynes, Kinney, Hellems, and Dexter[14] obstructed and distended a lobar pulmonary artery by dilating a balloon on the end of a venous catheter in that artery with a pressure higher than that in the main pulmonary artery. They were unable to note any constant change in the respiratory rate, pressure in the femoral and pulmonary arteries, and the heart rate of anesthetized and unanesthetized dogs. It is also important to note, accepting the minimal lethal dose of a 1:2 starch suspension established and presuming cornstarch and barium sulfate to be pulmonary embolic agents equal in all respects, that twice the dose of barium sulfate which is lethal when given into a peripheral vein was injected directly into each of two lobar pulmonary arteries at intervals of thirty minutes in three dogs anesthetized with chloralosane. Only one of these three dogs died and that was probably because heparin was omitted in the experiment. In the second series of injections of a selected lobar artery, death was produced in

one animal of six in which a slightly different procedure was used. That the mean systemic blood pressure was lowered in all animals and that this fall was the probable cause of death in one is interesting and suggestive, but inconclusive, evidence of reflex vasospasm in the pulmonary arterial system.

SUMMARY AND CONCLUSIONS

In these experiments it has been shown that:

1. A standard dose of a 1:2 suspension of cornstarch injected into a peripheral vein in heparinized rabbits will cause death in every instance, a fact that supports the work of de Takats, Beck, and Fenn,[3] and the conclusion that death is the result of lodgment of the starch particles in the arterioles and capillaries of the lungs and not in the heart or brain.

2. A similar standardization was established in anesthetized, heparinized dogs.

3. The result of such an injection was not altered by bilateral cervical vagotomy following bilateral sympathetic ganglionectomy from the stellate ganglion to the fifth thoracic ganglion in a series of dogs.

4. Death was produced in only one of six anesthetized, heparinized dogs from the forceful injection of a 1:1 suspension of insoluble barium sulfate into one, two, or three selected lobar pulmonary arteries.

5. In only one of six anesthetized, heparinized dogs was death caused by the slow injection of a 5:4 suspension of insoluble barium sulfate into a selected lobar pulmonary artery.

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ANNOUNCEMENT

Urology Award

The American Urological Association offers an annual award of $1,000 (first prize of $500, second prize $300, and third prize $200) for essays on the result of some clinical or laboratory research in urology. Competition shall be limited to urologists who have been in such specific practice for not more than five years and to residents in urology in recognized hospitals.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Hotel Statler, Washington, D. C., May 29-June 1, 1950.

For full particulars write the secretary, Dr. Charles H. de T. Shivers, Boardwalk National Arcade Building, Atlantic City, N. J. Essays must be in his hands before Feb. 20, 1950.

Book Reviews

Obstetric Analgesia and Anesthesia. By Franklin F. Snyder, M.D., Associate Professor of Obstetrics and Associate Professor of Anatomy, Harvard Medical School. Pp. 401, with 114 illustrations. Philadelphia, 1949, W. B. Saunders Company.

This is a critical review of the whole problem of the physiology and pharmacology of fetal respiration. A good case is established for the fact that interference with fetal respiratory mechanisms is responsible for a large part of neonatal mortality and morbidity. The author applies at length the techniques which he has used for the objective evaluation of the effect of drugs on the respiratory reflexes. This has been previously published but is brought together in this monograph and is related to the work of others. There is a somewhat brief discussion of the practical details of the various methods of analgesia and anesthesia in obstetrics.

This is an excellent book and contains information essential to anyone working in obstetrics. It is not a practical guide to obstetric analgesia and anesthesia. However, the theoretical background presented here is probably more useful. It is a welcome, authoritative, and condensed source of basic data.

Books Received

The receipt of books is acknowledged in this section and this treatment must be regarded as sufficient acknowledgment of the courtesy of the senders. Selections will be made for more extensive review dictated by the interests of our readers and as space permits.

MEDULLARY NAILING OF KUNTSCHER. By Lorenz Bohler, M.D., Professor of Surgery, University of Vienna. Cloth. Price $7. Ed. 1. Pp. 386, with 1,261 illustrations. Baltimore, 1948, Williams & Wilkins Company.

RECENT ADVANCES IN SURGERY. By Harold C. Edwards, C.B.E., M.S., F.R.C.S., Surgeon and Lecturer in Surgery, King's Hospital, London. Cloth. Ed. 3. Pp 437, with 131 illustrations. Philadelphia, 1948, The Blakiston Company.

THE THYROID AND ITS DISEASES. By J. H. Means, M.D., Jackson Professor of Clinical Medicine, Harvard Medical School. Cloth. Price $12. Ed. 2. Pp. 559, with 63 illustrations. Philadelphia, 1948, J. B. Lippincott Company.

NEUROSURGICAL PATHOLOGY. By I. Mark Scheinker, M.D., Assistant Professor of Neuropathology and Assistant Professor of Medicine (Neurology), University of Cincinnati. Cloth. Price $9.75. Ed. 1. Pp. 355, with 238 illustrations. Springfield, Illinois, 1948, Charles C Thomas, Publisher.

ABC'S OF SULFONAMIDE AND ANTIBIOTIC THERAPY. By Perrin H. Long, M.D., F.R.C.P., Professor of Preventive Medicine, Johns Hopkins University School of Medicine. Cloth. Ed. 1. Pp. 231, with no illustrations. Philadelphia, 1948, W. B. Saunders Company.

ROENTGEN STUDIES OF THE LUNGS AND HEART. By Nils Westermark, M.D., Director, Department of Radiology, St. Goran's Hospital, Stockholm, Sweden, edited by Leo G. Rigler, M.D., Professor of Radiology, University of Minnesota Medical School. Cloth. Price $7. Ed. 1. Pp. 216, with 98 illustrations. Baltimore, 1948, Williams & Wilkins Company.

ELEMENTARY ANESTHESIA. By William N. Kemp, M.D., C.M., Consultant Anesthetist, Children's Hospital, Vancouver, B. C. Cloth. Price $5. Ed. 1. Pp. 289, with 100 illustrations. Baltimore, 1948, Williams & Wilkins Company.

MANUAL OF UROLOGY. By Ralph M. LeComte, M.D., F.A.C.S., formerly Professor of Urology, Georgetown University. Cloth. Price $4. Ed. 4. Pp. 311, with 58 illustrations. Baltimore, 1948, Williams & Wilkins Company.

PEDIATRIC ANESTHESIA. By M. Digby Leigh, M.D., Director, Anesthesia, Vancouver General Hospital, and M. Kathleen Balton, M.D., Supervisor of Pediatric Anesthesia, Vancouver General Hospital. Cloth. Price $5.50. Ed. 1. Pp. 240, with 84 illustrations. New York, 1948, The MacMillan Company.

HOSPITAL TRENDS AND DEVELOPMENTS. By Arthur C. Bachmeyer, M.D., Director, University of Chicago Clinics, and Gerhard Hartman, Ph.D., Superintendent, University Hospitals, University of Iowa. Cloth. Price $5.50. Ed. 1. Pp. 819, with many illustrations. New York, 1948, Commonwealth Fund.

EMERGENCY SURGERY (PART I). By Hamilton Bailey, F.R.C.S. (Eng.), F.A.C.S., F.I.C.S., F.R.S.E., Surgeon-in-charge, Genito-Urinary Department, Royal Northern Hospital, London. Cloth. Price $5. Ed. 6. Pp. 180, with 289 illustrations. Baltimore, 1948, Williams & Wilkins Company.

EMERGENCY SURGERY (PART II). By Hamilton Bailey, F.R.C.S. (Eng.), F.A.C.S., F.I.C.S., F.R.S.E., Surgeon-in-charge, Genito-Urinary Department, Royal Northern Hospital, London. Cloth. Price $5. Ed. 6. Pp. 208, with 322 illustrations. Baltimore, 1948, Williams & Wilkins Company.

THE SURGERY OF THE STOMACH AND DUODENUM. By T. H. Somervell, M.A., M.B., B.ch., F.R.C.S., Surgeon-in-charge, London Mission Hospital, Neyyoor, S. India. Cloth. Ed. 1. Pp. 546, with many illustrations. Baltimore, 1948, Williams & Wilkins Company.

THE MODERN MANAGEMENT OF DUODENAL ULCER. By F. Croxon Deller, M.D., M.R.C.P. Cloth. Price $5.50. Ed. 1. Pp. 227, with many illustrations. Baltimore, 1948, Williams & Wilkins Company.

THE SURGERY OF ABDOMINAL HERNIA. By George B. Mair, M.D., F.R.E.P.S., F.R.C.S.E., Surgeon, Law Junction Hospital, Lanarkshire, England. Cloth. Price $7. Ed. 1. Pp 408, with many illustrations. Baltimore, 1948, Williams & Wilkins Company.

AN INTRODUCTION TO SURGERY. By Rutherford Morison, M.D., F.R.C.S. (Edin), Formerly Professor of Surgery, Durham University. Cloth. Price $10. Ed. 4. Pp. 330, with many illustrations. Baltimore, 1948, Williams & Wilkins Company.

OSTEO-ARTHRITIS OF THE HIP-JOINT. By H. Warren Crowe, D.M., B.ch., M.R.C.S., L.R.C.D., London. Cloth. Price $6.35. Ed. 1. Pp. 70, with many illustrations. London, 1948, George Pulman & Sons, Ltd.

ACUTE INTESTINAL OBSTRUCTION. By Rodney Smith, M.S., F.R.C.S., Assistant Surgeon, St. George's Hospital, London. Cloth. Price $5. Ed. 1. Pp. 258, with many illustrations. Baltimore, 1948, Williams & Wilkins Company.

TEXTBOOK OF ANESTHETICS. By R. J. Minnitt, M.D., D.A., (R.C.P.S.) Trinity College, Cambridge, and John Gillies, M.D., M.B., Ch.B., F.R.C.S., and D.A., Lecturer in Anesthetics, the University of Edinburgh. Cloth. Ed. 7. Pp. 567, with 227 illustrations. Baltimore, 1948, Williams & Wilkins Company.

STERILITY AND IMPAIRED FERTILITY. By Cedric Lane-Roberts, C.V.O., M.S., F.R.C.S., F.R.C.O.G., Gynecological Surgeon, Royal Northern Hospital, London, and associates. Cloth. Ed. 1. Pp. 400, with many illustrations. New York, 1948, Paul B. Hoeber, Inc.

FRACTURES AND DISLOCATIONS. By Edwin O. Geckler, M.D., F.A.C.S., Philadelphia, Pennsylvania. Cloth. Price $5. Ed. 4. Pp. 370, with 244 illustrations. Baltimore, 1948, Williams & Wilkins Company.

BRONCHIOGENIC CARCINOMA AND ADENOMA. By B. M. Fried, M.D., Attending Physician, Montefiore Hospital for Chronic Diseases, New York, New York. Cloth. Price $6. Ed. 1. Pp. 306, with 118 illustrations. Baltimore, 1948, Williams & Wilkins Company.

PLASTER OF PARIS TECHNIQUE. By E. O. Geckler, M.D., F.A.C.S., Professor, Orthopedic Surgery, Chief of Fracture Service, Hahnemann Medical College and Hospital,

Philadelphia. Cloth. Price $3. Ed. 2. Pp. 220, with 236 illustrations. Baltimore, 1948, Williams & Wilkins Company.

AN INTRODUCTION TO GASTROENTEROLOGY. By Walter C. Alvarez, Professor of Medicine, University of Minnesota, The Mayo Foundation, Rochester. Cloth. Price $12.50. Ed. 4. Pp. 903, with 269 illustrations. New York, 1948, Paul B. Hoeber, Inc.

PARATHYROID GLANDS AND METABOLIC BONE DISEASE. By Fuller Albright, M.D., A.B., Associate Professor of Medicine, Harvard Medical School, Boston, and Edward C. Reifenstein, Jr., A.B., M.D., F.A.C.P., Consultant-in-charge, Department of Clinical Investigation, Sloan-Kettering Institute of Cancer Research, Memorial Hospital Cancer Center, New York. Cloth. Price $8. Ed. 1. Pp. 393, with 157 illustrations. Baltimore, 1948, Williams & Wilkins Company.

OBSTETRIC ANALGESIA AND ANESTHESIA. By Franklin P. Snyder, M.D., Associate Professor of Obstetrics and Associate Professor of Anatomy, Harvard Medical School. Cloth. Ed. 1. Pp. 401, with 114 illustrations. Philadelphia, 1949, W. B. Saunders Company.

BLOOD TRANSFUSION. By Elmer L. DeGowin, M.D., Associate Professor of Internal Medicine, State University of Iowa. Cloth. Price $9. Ed. 1. Pp. 587, with 200 illustrations. Philadelphia, 1949, W. B. Saunders Company.

MAYO CLINIC DIET MANUAL. By Committee on Dietetics of Mayo Clinic, Rochester, Minnesota. Paper. Price $4. Ed. 1. Pp. 329, with no illustrations. Philadelphia, 1949, W. B. Saunders Company.

THE BUSINESS SIDE OF MEDICAL PRACTICE. By Theodore Wiprud, Executive Director and Secretary, Medical Society of District of Columbia. Cloth. Price $3.50. Ed. 2. Pp. 232, with 22 illustrations. Philadelphia, 1949, W. B. Saunders Company.

DEEP MASSAGE AND MANIPULATION. By James Cyriax, M.D., Department of Physical Medicine, St. Thomas' Hospital, London. Cloth. Price $5. Ed. 3. Pp. 274, with 104 illustrations. Great Britain, 1948, Gray and Gray Company.

CLINICAL ASPECTS AND TREATMENT OF SURGICAL INFECTIONS. By Frank Lamont Meleeney, M.D., F.A.C.S., Associate Professor of Clinical Surgery, Columbia University, New York. Cloth. Price $12. Ed. 1. Pp. 840, with many illustrations. Philadelphia, 1949, W. B. Saunders Company.

TEXTBOOK OF GENITO-URINARY SURGERY. By H. P. Winsbury-White, M.B., Ch.B., F.R.C.S., Surgeon, St. Paul's Hospital for Genito-Surgery Diseases, London. Cloth. Ed. 1. Pp. 1,046, with many illustrations. Baltimore, 1949, Williams & Wilkins Company.

NEURORADIOLOGY. By Alexander Orley, M.D., F.F.R., Honorable Consulting Radiologist, West End Hospital for Nervous Diseases, London. Cloth. Price $11.50. Ed. 1. Pp. 436, with 587 illustrations. Springfield, 1949, Charles C Thomas, Publisher.

ATLAS OF PERIPHERAL NERVE INQUIRIES. By William R. Lyons, Ph.D., Associate Professor of Anatomy, University of California Medical School, and Barnes Woodhall, M.D., Professor of Neurosurgery, Duke University, Durham, North Carolina. Cloth. Ed. 1. Pp. 340, with 135 illustrations. Philadelphia, 1949, J. B. Lippincott Company.

TUMORS OF BONE. By Charles F. Geschickter, M.D., Professor of Pathology, Georgetown University Medical School. Cloth. Price $17.50. Ed. 3. Pp. 810, with 642 illustrations. Philadelphia, 1949, J. B. Lippincott Company.

NURSING CARE OF NEUROSURGICAL PATIENTS. By Roland M. Klemme, M.D., F.I.C.S., F.A.C.S., Professor, Department of Surgery, St. Louis University School of Medicine. Cloth. Price $3. Ed. 1. Pp. 134, with 69 illustrations. Springfield, 1949, Charles C Thomas, Publisher.

THE 1948 YEARBOOK OF NEUROLOGY, PSYCHIATRY, AND NEUROSURGERY. By Hans H. Reese, M.D., Professor of Neurology and Psychiatry, University of Wisconsin Medical School, Nolan D. Lewis, M.D., Director, New York State Psychiatric Institution and Hospital, Percival Bailey, M.D., Professor of Neurology and Neurological Surgery, University of Illinois. Cloth. Price $5. Ed. 1. Pp. 750, with 140 illustrations. Chicago, 1949, Williams & Wilkins Company.

THE PRINCIPLES AND PRACTICE OF RECTAL SURGERY. By William B. Gabriel, M.S., F.R.C.S., Surgeon, St. Mark's Hospital, London. Cloth. Price $14.50. Ed. 4. Pp. 518, with 278 illustrations. Springfield, 1948, Charles C Thomas, Publisher.

BRITISH SURGICAL PRACTICE, VOLUME III. By Sir Ernest R. Carling, F.R.C.S., F.R.C.P., Consulting Surgeon, Westminster Hospital and J. Paterson Ross, M.S., F.R.C.S., Surgeon and Director of Surgical Clinical Unit, St. Bartholomew's Hospital, London. Cloth. Ed. 1. Pp. 524, with 291 illustrations. St. Louis, Missouri, 1949, The C. V. Mosby Company.

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NEOPLASMS OF BONE AND RELATED CONDITIONS. By Bradley L. Coley, Attending Surgeon, Bone Tumor Department, Memorial Hospital, New York. Cloth. Price $17.50. Ed. 1. Pp. 800, with 622 illustrations. New York, 1949, Paul B. Hoeber, Inc.

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PLASTIC SURGERY OF THE NOSE. By Albert P. Seltzer, M.D., M.Sc., Sc.D., F.I.C.S., F.A.C.S., Associate in Otolaryngology, University of Pennsylvania Medical School. Cloth. Price $12. Ed. 1. Pp. 305, with 221 illustrations. Philadelphia, 1949, J. B. Lippincott Company.

MEDICINE THROUGHOUT ANTIQUITY. By Benjamin L. Gordon, M.D., Attending Opthalmologist, Shore Memorial Hospital, Somers Point, New Jersey. Cloth. Price $6. Ed. 1. Pp. 818, with 157 illustrations. Philadelphia, 1949, F. A. Davis Company.

PRACTICAL ASPECTS OF THYROID DISEASE. By George Crile, Jr., M.D., Department of Surgery, Cleveland Clinic, Cleveland, Ohio. Cloth. Price $6. Ed. 1. Pp. 355, with 101 illustrations. Philadelphia, 1949, W. B. Saunders Company.

HANDBOOK OF SURGERY. By Eric C. Mekie, M.B., Ch.B., F.R.C.S. (Edin), F.I.C.S., Professor of Clinical Surgery, King Edward VII College of Medicine, Singapore, and Ian MacKenzie, M.B.E., M.B., Ch.B., F.R.C.S. (Edin), First Assistant, Department of Surgery, University of Durham. Cloth. Ed. 2. Pp. 764, with 29 illustrations. Baltimore, 1949, Williams & Wilkins Company.

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A SURGEON'S GUIDE TO LOCAL ANESTHESIA. By C. E. Corlette, M.D., Ch.M., F.R.A.C.S., Consulting Surgeon, Balmain Hospital, Sydney, Australia. Cloth. Price $8.50. Ed. 1. Pp. 355, with 200 illustrations. Springfield, 1949, Charles C Thomas, Publisher.

HOW TO BECOME A DOCTOR. By George R. Moon, A.B., M.A., Examiner and Recorder, University of Illinois Colleges of Medicine, Dentistry & Pharmacy. Cloth. Price $2. Ed. 1. Pp. 131, with no illustrations. Philadelphia, 1949, The Blakiston Company.

THE TECHNIQUE OF PULMONARY RESECTION. By Richard H. Overholt, M.D., Clinical Professor of Surgery, Tufts Medical School, and Lazaro Langer, M.D., Instructor in Surgery, University of Cordoba, Argentina. Cloth. Price $8. Pp. 208, with 133 illustrations. Springfield, 1949, Charles C Thomas, Publisher.

ATLAS OF ORAL AND FACIAL LESIONS. By Ralph H. Brodsky, Consulting Oral Surgeon, Department of Hospitals, New York City. Cloth. Price $80, with 100 color slides. Ed. 1. Pp. 129, with 100 illustrations. Baltimore, 1948, Williams & Wilkins Company.

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PATHOLOGY AND SURGERY OF THYROID DISEASE. By Joseph L. DeCourcy, M.D., Senior Surgeon, Good Samaritan Hospital, and Cornelius B. DeCourcy, M.D., Member, DeCourcy Clinic Surgical Staff, Cincinnati, Ohio. Cloth. Price $10. Ed. 1. Pp. 476, with 93 illustrations. Springfield, Illinois, 1949, Charles C Thomas, Publisher.

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EXPERIMENTAL SURGERY. By J. Markowitz, M.B.E., M.B. (Tor.), Ph.D., M.S., Associate Professor of Physiology, University of Toronto. Cloth. Price $7. Ed. 2. Pp. 546, with 330 illustrations. Baltimore, 1949, Williams & Wilkins Company.

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SURFACE AND RADIOLOGICAL ANATOMY. By A. B. Appleton, M.A., M.D. (Cantab.), Professor of Anatomy, University of London, W. J. Hamilton, M.D., D.Sc., F.R.S.E., Professor of Anatomy, University of London, and G. Simon, M.D., B.Ch., D.M.R.E. (Cantab.), Demonstrator of Radiological Anatomy in the Medical College of St. Bartholomew's Hospital. Cloth. Price $9. Ed. 3. Pp. 332, with 390 illustrations. Baltimore, 1949, Williams & Wilkins Company.